

**Presence and impact of bleeding from the mouth
in people living with Von Willebrand's disease in
Ireland**

A thesis submitted for the degree of Master in Dental Science by

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Declaration

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Summary

Von Willebrand Disease (vWD) is one of the most common congenital bleeding disorders (CBD). Mucosal bleeding is a feature of vWD. This includes menorrhagia, nosebleeds and bleeding from the gums. It has been documented that people with vWD and the teams who treat them believe that such gum bleeding is inevitable and associated with the bleeding disorder. There is some evidence that people with vWD do not seek care until there is a severe impact on their quality of life. There is currently little evidence available to determine whether gum bleeding in vWD is inflammatory gingivitis or indeed mucocutaneous bleeding. The aims of the study were a) to describe the presence and impact of bleeding from the mouth in people living with vWD and b) to explore the association between plaque-induced gingivitis and objective measures of vWD.

A consecutive sample of N = 24 people (achieved sample 43% of target) with vWD attending a Haematology outpatient clinic at St James Hospital Dublin agreed to participate in the study. Data were gathered between the 17th May 2018 and the 4th March 2019. A validated questionnaire was completed by participants which assessed self-report of health, oral health related quality of life, oral health behaviours, dental anxiety, perception and experience of gingival bleeding. Bivariate analyses were performed assessing the association between gingival health (Gingival Index, Modified Bleeding Papillary Index) and plaque levels and i) self-report of bleeding ii) clinical markers for a bleeding disorder in vWD (von Willebrand Factor Antigen and Ristocetin Cofactor).

Participants mostly rated their general health (92%) and oral health (71%) respectively as 'good' or 'very good', but a proportion (19%) only considered their oral health to be fair. Participants reported they experienced a mean of 3.2 (SD 3.0) impacts per person assessed through Oral Health Impact Profile-14 with the most frequent impacts related to three items: painful aching in the mouth (33%); difficulty in relaxing (33%) and discomfort when eating (30%). When participants were asked to self-report factors contributing to reduced quality of life three main issues were reported: toothache (65%), tooth sensitivity (50%) and bleeding gums (33%). Self-report of oral health behaviours were mostly positive (smoking, sugar consumption and dental attendance). Oral hygiene practices were optimal though plaque accumulation was high, and all participants had mild and moderate gingivitis assessed through GI (0.4 SD 0.7) and MBPI (7.3 SD 7.2).

Participants were generally unconcerned about the presence of bleeding gums though a small proportion reported concerns. No participants attributed bleeding gums to their bleeding disorder. Rather, most participants attributed the presence of bleeding to tooth brushing techniques or to the issue of hard brushes. Most acknowledged that they had little understanding of why their gums bled but felt that treatment (dental) would be beneficial.

Bivariate analyses showed a small to moderate correlation between plaque levels and GI and MBPI respectively, but this was not significant. The under powering of the sample may have confounded the relationship. In contrast there was no correlation between objective measures of gingival bleeding and objective

markers of low vWD, suggesting there was no relationship between bleeding disorder and gingival bleeding.

Given the limitations of the present study in terms of sample size, it may be concluded tentatively that there is no association between gingival bleeding and vWD factor suggesting the most likely cause of gingival bleeding is suboptimal plaque control. Oral hygiene interventions are warranted in this population subgroup.

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Chapter One: Introduction

1.1 Introduction

Bleeding disorders are described as conditions with impaired haemostatic process; they can be congenital or acquired conditions. The most common congenital bleeding disorders (CBD) are von Willebrand disease (vWD), Haemophilia A and Haemophilia B which account for 95-97% of all coagulation deficiencies (Vassilopoulos & Palcanis, 2007). In high-income countries there has been a dramatic change in the management and life expectancy of people living with CBD (Ahmad *et al.*, 2013). This is largely due to the development of factor replacement therapy either through weekly prophylaxis or 'on demand' factor as appropriate when a specific planned bleeding episode is anticipated e.g. surgery (Ahmad *et al.*, 2013). The picture is more complicated in low- and middle-income countries where access to factor is less reliable or non-existent. The experience in countries where access to factor is readily available has been to increase life expectancy and quality of life through increased participation in daily activities such as education, employment and social life for people with CBD. This change is well illustrated in oral health where in the past people with CBD required hospitalisation and complex management if dental care was needed. Dental care was often avoided and neglected (WFH, 2006). Now it is understood that even in the presence of a severe bleeding disorder many dental procedures such as restorative dentistry, endodontics and supra gingival calculus removal do not require factor replacement (UKHCDO, 2013). Despite the evidence there still remain some concerns amongst people living with CBD and their haematology teams in relation to bleeding associated with periodontal disease and some

dental procedures. This is probably due to the medical and dental professions' tendency to catastrophise any dental procedure and the lack of knowledge of dentistry amongst haemophilia teams (Rahman *et al.*, 2019). There is limited evidence that people with CBD also hold these outdated views and attribute gingiva bleeding to their bleeding disorder rather than plaque induced gingivitis (Hitchings *et al.*, 2012). These views have led people to stop brushing their teeth and to avoid dental care to the extent that when they do seek dental care it needs to be invasive (involving tooth extractions). In turn poor oral health might consequently require invasive dental treatment, therefore increasing the chance of prolonged post-operative bleeding (Scully *et al.*, 2014). Dental diseases may be prevented or reversed in their early stage (Fejerskov *et al.*, 2013). As regular effective oral hygiene is central to this, it is important that people with CBD should be exposed to dental prevention throughout the life course to alleviate their risk of oral disease. In order to do this, we must understand what people with CBD believe about bleeding gums and how closely their assessment of their own gums align with objective measures.

Chapter Two: Literature review

2.1 Congenital bleeding disorders sources of literature

In order to provide a comprehensive review, the literature was searched for papers in relation to CBD. The following mesh terms were used oral health, oral health related quality of life, congenital bleeding disorders, von Willebrand disease, gingival bleeding, management, consort, dental needs, access, barriers, oral hygiene, behavioural change, behavioural interventions, gingival index, bleeding index, plaque index, plaque-induced gingivitis, periodontitis, health related quality of life.

2.1.1 Haemostasis

Haemostasis is the physiological process of stopping bleeding at the injury site by formation of a haemostatic plug (Gale, 2011). There are two phases, primary and secondary haemostasis. Primary haemostasis activates platelet aggregation and their adhesion, which is facilitated by von Willebrand factor (vWF) (Yun *et al.*, 2016). vWF forms the bridge between platelet's glycoprotein 1b and exposed collagen at the site of injury (Yun *et al.*, 2016). The secondary stage of haemostasis involves the stimulation of formation of insoluble fibrin through the coagulation cascade (Gale, 2011). Normal haemostasis involves simultaneous response and interaction of vessels, platelets, localised coagulation of fibrin and its deposition (Mickie & Bull, 1989). Primary haemostasis starts with immediate vasoconstriction of cells upon injury. This vasospasm is to keep the blood coagulation in a localised area (von Ommen & Peters, 2011). Through glycoprotein (GP) receptors platelets interact and gather in the injured area, with

vWF bridging their mediation and firmer adhesion follows (Rick *et al.*, 2003). See Figure 1.

vWF's primary role is to stimulate thrombus formation by facilitating adhesion of platelets, but it is also a carrier for factor VIII (Ruggeri, 1997). When platelet granules are released, the content of granules subsequently cause activation of the coagulation reaction (von Ommen & Peters, 2011). Abnormalities at this stage of haemostasis – (vWF, platelet number or function) causes mucosal bleeding: gingival bleeding, melaena, petechiel etc (Scully *et al.*, 2014).

Secondary haemostasis starts with the extrinsic pathway and release of tissue factor (TF). Then TF activates factor VIIa, which activates a small quantity of factors IX and X (Hoffman, 2003). This Xa forms a prothrombinase structure. A small quantity of thrombin is generated, and acceleration of clotting process and platelets aggregation occur. During this activation, factors V and VIII, XI and XIa are released. FIXa binds to FVIIIa on the platelet surface, it forms a structure that provides factor Xa (Hoffman, 2003). Once platelet prothrombinase aggregation is completed, the thrombin bursts and a fibrinogen clot is formed (Hoffman, 2003).

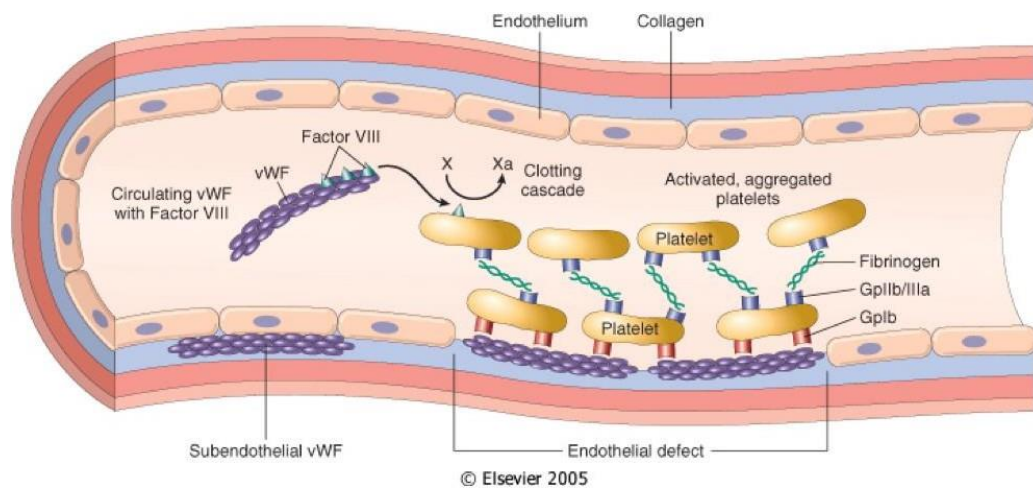


Figure 1 Function of VWF (Memorang, 2017) Source: Elsevier, 2005

2.1.2 Definition of a congenital bleeding disorder

Congenital bleeding disorders (CBD) are inherited disorders, which include a range of disorders that affect vascular, platelet or clotting factors (Vassilopoulos & Palcanis, 2007). In the platelet and vascular disorders, bleeding occurs immediately as a part of the initial response to an insult or injury. People present with mucocutaneous bleeding such as nose bleeds, purpura, menorrhagia etc. (Ali *et al.*, 2018). In contrast with a clotting disorder, the vascular and platelet responses are usually normal or near normal and may mask the problem initially (Scully *et al.*, 2014). As the clotting response occurs last (in fact in this group it is delayed) these people experience delayed bleeding, which can then progress to cause haemorrhage in joints and soft tissues (Ali *et al.*, 2018).

The most common CBDs are vWD, Haemophilia A and B. and are caused by defective or a lack of a certain haematological factor (Rafique *et al.*, 2013).

Haemophilia A or Factor VIII deficiency accounts for almost 85% of all Haemophilia cases (Anderson *et al.*, 2013). It is characterised by deficiency of factor VIII (FVIII). It affects males mainly, where sons of carriers present a 50:50 risk of developing Haemophilia A, and daughters a 50:50 risk of being carriers (Scully *et al.*, 2007).

Haemophilia B is characterised by a defect of factor IX. It is a sex-linked genetic disorder. The gene is carried on the X chromosome. This type of haemophilia can only be passed on by affected mothers (Anderson *et al.*, 2013).

vWD is characterised by a defective or abnormal plasma protein vWF (Sadler, 2003). vWF stabilises FVIII and facilitates platelet interaction with the injured vessel wall (Mackman *et al.*, 2007). More details of vWD are provided in a later section (2.1.3).

2.1.3 Von Willebrand Disease

Von Willebrand Disease represents the most common inherited bleeding disorder in man and is caused by either a deficiency or dysfunction of the plasma protein vWF. It is estimated that 1% of the population is affected (Lavin *et al.*, 2017; Abed & Ainousa, 2017). vWD is an autosomal dominant condition, which affects both sexes (Anderson *et al.*, 2013). There are different subtypes of vWD with each displaying different clinical features.

Type of vWD	Deficiency	Clinical features
Type 1	Partial quantitative deficiency of vWF	Commonest form of vWD; generally, mild bleeding symptoms
Type 2 (4 subtypes A,B,M,N)	Qualitative deficiency of vWF	Bleeding after surgery or tooth extraction; mucocutaneous bleeding
Type 3	Complete quantitative deficiency of vWF	Severe symptoms of bleeding; mucocutaneous bleeding

Table 1 Types of vWD and clinical features. Source: (Weickert et al., 2014)

vWF is a glycoprotein (GP) that is present in plasma and vessel walls. It is a carrier for Factor VIII and serves as protecting factor from proteolytic degradation, therefore increasing FVIII's half-life. FVIII is required for platelet adhesion to an injured endothelium and platelet aggregation. vWF forms a structure with FVIII to stabilise this factor in the circulation (Holmberg & Nilsson,1992). Thus, a deficiency in vWF leads to a lower concentration of FVIII in the blood. Factor VIII antigen (Ag)-vWF which binds platelets, ristocetin co-factor vWF: RCo helps platelets aggregation and factor VIII clotting activity(C)- participates in clotting cascade (James & Goodeve, 2011). Therefore, a deficiency of vWF leads to a lack of platelet adhesion (Ng et al., 2015).

Type I vWD is characterised by quantitative reduction of normal vWF, vWF: Ag at levels of 1-50 IU/dL. It accounts for most of the cases of vWD disease around 75% (Lavin et al., 2017). Type II represents abnormal function in vWF and

accounts for 25% of vWD cases (Lavin *et al.*, 2017). Type III is very rare and represents patients with complete absence of vWF (Lavin *et al.*, 2017). The bleeding symptoms experienced may be explained by poor platelet aggregation, thus explaining the prolonged bleeding time (Scully *et al.*, 2014).

The bleeding phenotype of vWD is important and helps identify the treatment and/or prophylaxis required. The International Society on Thrombosis and Haemostasis (ISTH) developed a questionnaire that quantifies bleeding symptoms - Bleeding Assessment Tool (BAT). This questionnaire distinguishes healthy subjects and people with vWD and is used to elicit bleeding phenotype (Rodeghiero *et al.*, 2010).

The most common clinical manifestations for vWD is bleeding from mucocutaneous tissues: nose bleeds, oral bleeding and menorrhagia (Sadler, 2003; Tosetto *et al.*, 2005). Gingival bleeding is reported to be more common in vWD when compared to Haemophilia A and B (Rafique *et al.*, 2013).

Data from the cohort Low Von Willebrand Factor (Lovic) study has advanced understanding of the pathophysiology of type I vWD and what has been termed low vWF (Lavin *et al.*, 2017). These findings propose to differentiate between Type I vWD (plasma vWF: Ag levels <30IU/dL) from low vWF (30-50 IU/dl). Importantly individuals with vWD may have low levels of vWF but they also continue to express a bleeding phenotype (Lavin *et al.*, 2017). Concomitant haemostatic abnormalities however do not explain bleeding phenotype in low VWF. The mechanism for production of low levels of vWF is not fully understood

but is believed to involve a combination of reduced synthesis and accelerated plasma vWF clearance (Lavin *et al.*, 2017).

Laboratory and clinical testing include vWF antigen level and activity (ristocetin and collagen binding), factor VIII activity and bleeding time. Once vWD is diagnosed, additional tests for vWF multimer and ristocetin (induced platelet aggregation (RIPA)) are performed (Rick *et al.*, 2003).

2.1.3.1 *Therapy*

The main treatment modalities for patients with vWD are:

- Tranexamic acid - inhibits fibrin clot lysis, is given systemically and locally (mouth rinses, gels) (Eghbali *et al.*, 2016) (e.g. Cyklokapron).
- Desmopressin (synthetic antidiuretic hormone) stimulates release of endogenous factor FVIII and vWF from stores (Federici, 2008). It is given via nasal spray. Although contraindicated in type IIB and III (Anderson *et al.*, 2013) (e.g. DDAVP).
- Clotting factor VIII replacement therapy. This factor is delivered intravenously 30 minutes – one hour prior to the procedure (Sharma & Flood, 2017; Anderson *et al.*, 2013) (e.g. Advate).
- Prophylaxis with intermediate purity of FVIII or high purity of VWF for recurrent bleeding may be considered (Laffan *et al.*, 2014) (e.g. Wilate).

2.1.3.2 *Proposed dental management*

Invasive procedures such as dental extractions, oral surgery, periodontal surgery, implants placement, root debridement procedures usually require haemostatic support (Anderson *et al.*, 2013). The decision to use local or systemic support is

largely dependent on the severity of vWD (Scully *et al.*, 2014). Recent evidence suggests that inferior dental blocks and buccal and palatal infiltrations may be given without adverse events using standardised techniques (Dougall *et al.*, 2019).

Pain control may be achieved by using local anaesthetic with vasoconstrictor either lidocaine 1:80.000 epinephrine or articaine 1:100.000 epinephrine. Injections in the floor of the mouth should be avoided because of possible obstruction of airway (Scully *et al.*, 2014; Anderson *et al.*, 2013).

2.2 Oral health status

The World Health Organisation defines health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (WHO, 2018). Oral health is an integral part of health and is an indicator for overall wellbeing.

“Oral health is multi-dimensional in nature including physical, psychological, emotional and social domains integral to overall health and well-being. Oral health is subjective and dynamic in nature enabling individuals to perform essential functions including eating, speaking, smiling and socialising without discomfort, pain or embarrassment. Good oral health reflects an individual's ability to adapt to physiological changes throughout life and to maintain their own teeth and mouth through self-care in an autonomous and independent fashion “(Peres *et al.*, 2019, p. 2).

Oral diseases such as dental caries, periodontal diseases, oral cancers etc. account for a significant disease burden worldwide only less burdensome globally than arthritis and back pain (Kassebaum, 2017). Most dental diseases are largely preventable or can be successfully treated and arrested at their early stage (WHO, 2018).

2.2.1 Periodontal disease

Periodontal health can be described as a condition that is free from inflammatory periodontal disease and allows a person to function normally, without suffering any consequences, as a result of past disease (Lang & Bartold, 2018). Periodontal disease is the most common chronic inflammatory condition in humans (Chapple & Genco, 2013). It affects 50% of the world's population and 83% of the European population present with some level of periodontal inflammation (Chapple & Genco, 2013).

2.2.2 Gingivitis and periodontitis

Initiation of gingivitis is believed to be plaque-induced. Accumulation of undisturbed plaque within a few days leads to an initial lesion of gingival inflammation (Loe *et al.*, 1965). Gingivitis is confined to inflammation in free and attached gingiva, without extending beyond the mucogingival junction and is fully reversible (Murakami *et al.*, 2018). The commonest clinical signs of plaque-induced gingivitis are erythema, oedema, bleeding and gingival enlargement (Tonetti *et al.*, 2015).

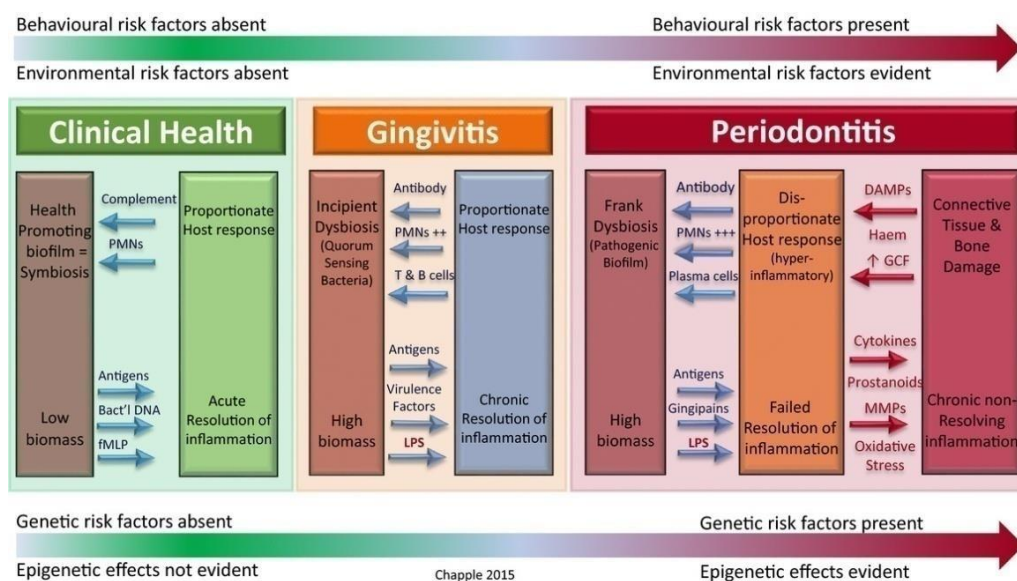


Figure 2 Contemporary model of host-microbe interactions in the pathogenesis of periodontitis (Meyle & Chapple, 2015)

Gingival inflammation is a necessary precondition for further destructive progression to periodontitis and tooth loss though this is not inevitable (Kinane & Attstrom, 2005). Periodontitis is defined as microbially-associated, host-mediated inflammation that results in destruction of tooth-supporting apparatus. It enables loss of marginal periodontal ligament fibres and apical migration of junctional epithelium which promotes apical spread of the bacteria along the root surface (Tonetti *et al.*, 2018).

A shift in microbial composition occurs here with emerging pathogenic bacteria, resulting in host tissue damage (Teles *et al.*, 2012). Periodontitis is a major health problem; it can lead to tooth loss, negatively affecting eating and aesthetics, quality of life and general health (Papapanou *et al.*, 2018). Plaque removal procedures when performed adequately and at regular intervals can reliably control the plaque biofilm (Loe *et al.*, 1965).

2.2.2.1 The importance of early detection and prevention

Bleeding on probing (BOP) parameters are best used for monitoring healthy or inflamed tissues (Lang *et al.*, 1996). Sites that bleed on light pressure (0.25 N) are associated with early signs of gingival inflammation (Lang *et al.*, 1991). Loe *et al.*, 1965 in their study demonstrated the development of gingivitis in healthy individuals in the absence of oral hygiene measures by the third week of abstention from oral hygiene measures. The Gingival Index (Loe & Silness, 1963) (to detect bleeding) and the Plaque Index System (Silness & Loe, 1964) (to detect plaque accumulation) were used for clinical examination in Loe's research. Bacterial data were collected and recorded until all subjects were diagnosed with gingivitis. By this time, bacterial load and the number of leukocytes had increased significantly. Once clinical gingivitis was observed an oral hygiene routine was reinstated and gingival inflammation was shown to resolve within 10 days. Thus, gingivitis can be regarded as a relatively nonspecific inflammatory response to nonspecific microbiota and reversible (Teles *et al.*, 2012).

2.2.2.2 Periodontal instrumentation

Plaque removal and calculus removal remains the cornerstone of professional management of the gingival tissues to reduce biological load, inflammation and plaque retaining features respectively (Tonetti *et al.*, 2015). According to Tonetti *et al.*, 2015, professional mechanical plaque removal (PMPR) is recommended and calculus removal is deemed to be essential for patient's adequate self-performed oral hygiene.

Needleman *et al.*, 2015 showed in their systematic review that PMPR with Oral Hygiene Instructions has more benefit in reduction of plaque and gingival inflammation than no treatment. However, when PMPR with Oral hygiene instructions (OHI) was compared with OHI alone, there appeared to be no additional benefit from PMPR when there is adherence with OHI.

2.2.3 Periodontal disease and CBD

There is little known about the oral health of people with CBD. A single small study in the UK suggested they had a higher levels of plaque accumulation by 34%, calculus and bleeding on probing by 23% and 38% respectively when compared to the general population (Moosajee *et al.*, 2013). It was also noted that bleeding from the mouth was mostly attributable to gingivitis and not to the CBD (Moosajee *et al.*, 2013). The authors concluded that patients avoided tooth brushing because the bleeding associated with oral hygiene was attributed erroneously to their bleeding disorder. In contrast, Weickert *et al.*, 2014 demonstrated a higher Gingival Bleeding Index (GBI) of 12.2% in a control group compared to the group with vWD, 10%. There was no difference between these two groups in Bleeding on Probing (BOP) index.

2.2.4 Periodontal disease and vWD

Although gingival bleeding is a frequently reported symptom of vWD there is no evidence yet connecting this bleeding disorder with more pronounced bleeding from gingivitis or with mucocutaneous bleeding. A case control study reported higher gingival bleeding in a control group compared to vWD. This study failed to find significant differences in bleeding on probing between controls and those with vWD (Weickert *et al.*, 2014).

2.2.5 Caries experience and CBD

Moosajee *et al.*, 2013 in their study in UK demonstrated that patients with CBD had a higher level of coronal caries (43 %) when compared to general population. Ziebolz *et al.*, 2011 when undertaking a study in Germany confirmed an increased level of DMFT and dmft scores in those with a CBD. Table 2 compares the oral health between people with CBD and the general population from three studies; two from Germany and one from England. These were three of the few studies which reported an oral health and compared people with CBDs with the general population.

Table 2 Comparison (Germany and England) of Oral Health between individuals with a CBD and general population from three studies.

Author and date	Ziebolzet <i>et al.</i> ,2011	Weickeret <i>et al.</i> , 2014	Moosajee <i>et al.</i> , 2013
Study design	Case control study, Germany	Case control study, Germany	Cross-sectional, observational study in England
Number of people	15 with CBD V 31 non-affected controls	50 with vWD V 40 healthy controls	18 with CBD V dentate adults in UK, 2009
Participants	Haemophilia A (53%), vWD type 2 a (47%).	Type 1 vWD	Haemophilia A (72%) vWD Type 1 and 2 (28%)
Age	18-60	18-80	16-70
Clinical Measures	DMFT Modified Quigley-Hein Index (MQHI), Panoramic X-ray (alveolar bone loss)	Modified Gingival Bleeding Index (GBI), Modified Plaque Index (PI), PPD & recession	DMFT Visible Plaque, PPD, Bleeding on Probing (BOP), Tooth wear in anterior teeth
Compared with the general Population Y/N	Yes	Yes	Yes
Results	Median of DMFT > by 3 in sample than controls, Median of alveolar bone loss > by 0.73 in sample than control, Median of MQHI score without difference (0.03) between sample & control.	GBI < by 2% in vWD than control, BOP < 0.2% in vWD than control, PI > 0.8% in vWD than control Similar findings in PPD	Coronal caries 43% > in sample group than general population, Visible Plaque 34% > in sample group than in general population, PPD "greater than 4 mm" in sample group 22% < than in general population, BOP > 38% in sample group than general population, Tooth Wear < 27% in sample group than general population

2.2.6 Oral hygiene

Much of the higher rates of oral diseases seen in people with CBD may well be attributable to low adherence with oral hygiene regimes and regular dental treatment (Fiske *et al.*, 2002). In a New Zealand study, patients with haemophilia stopped brushing their teeth in the presence of gingivitis (thus prolonging gingivitis) as they attributed the bleeding to their bleeding disorder, rather than to the presence of dental plaque (Hitchings, 2012). In the UK, the majority of patients in one small London study did recall receiving information on the prevention of dental disease, but often it was received too late or not put into practice (Fiske *et al.*, 2000).

2.2.7 Quality of life

Poor oral health in the general population has a huge impact on a patient's quality of life, causing not only physical, but psychological and social problems (Nutall *et al.*, 2011). There is a loss of self-image and self-esteem, as well as anxiety and depression (NIH, 2014). In a report in the UK, almost 70 % of adults with CBD reported that their lives were limited by their condition. They expressed concerns with impaired mobility and the consequences of acquiring HIV, Hep B and/or Hep C. These transmitted diseases negatively affected oral health: salivary gland disease, xerostomia, glossitis, periodontal lesions etc. People had also experienced problems accessing dental care (Fiske *et al.*, 2000).

According to Moosajee *et al.*, 2013 almost all participants in their small London study reported that they had impaired oral health related quality of life, as assessed using OHIP14 (Slade, 1997), when compared to the general

population. They also felt that they were at risk for tooth decay, periodontal disease and tooth wear.

2.3 Access to dental care

People with CBD face many barriers to dental care. According to Fiske *et al.*, (2000) half of the participants in their study preferred to be treated in specialist dental centres. While specialist care increases patients' confidence and delivers high standard of targeted care, for most people it involves travelling long distances (Fiske, 2000). Subsequently, it might increase financial costs and be a great inconvenience (Fiske *et al.*, 2002).

Most people with CBD feel that there is a lack of understanding amongst the public regarding their disorder (Barlow *et al.*, 2007). Due to the 'stigma' attached, and to perceived assumptions and stereotypes, people are very careful about informing others about their bleeding disorder (Barlow *et al.*, 2007). Even though more than half of the people with CBD in one UK study received regular dental care another one third experienced some problems accessing dental care with general dentists (Fiske *et al.*, 2000). General dental practitioners (GDPs) are reportedly not confident in the dental management of patients with bleeding disorders, they feel anxious to treat them or they have had bad previous experience when treating them (Kalsi *et al.*, 2012). Patients are extremely concerned about dentists' understanding of their bleeding condition and their knowledge of its management (Fiske *et al.*, 2000). Some patients reported being refused care by local dental practitioners for the reason of their bleeding disorders (Kalsi *et al.*, 2012).

2.4 Dental fear/anxiety

The greatest barrier resulting in CBDs patients not seeking dental attention is dental fear. A major fear for patients is the risk of bleeding either during or after treatment and fear of being hurt (Fiske *et al.*, 2000). More than a third of the participants followed in one UK study experienced problems after dental treatment: postoperative bleeding, bruising and swelling (Fiske *et al.*, 2000). The older generation who have contracted HIV and/or the Hepatitis virus also report experiencing some form of anxiety and difficulty in disclosing their status (Dougall & Fiske, 2008).

2.5 Importance of prevention

Dental treatment may require modification according to the haemostatic disorder. In severe cases this may involve multiple visits and expensive replacement factor therapy (Gomez-Moreno *et al.*, 2005). Patients with regular dental attendance patterns are less likely to require extractions and invasive dental treatment (Kalsi *et al.*, 2012). Delaying dental treatment could lead to the need for invasive dental procedures, with the potential of complications such as prolonged bleeding and haematoma formations in the neck area (Scully & Cawson, 2005).

Fiske *et al.*, 2002 demonstrated the need for the prevention of periodontal disease and caries, as almost all participants with CBD in their study required periodontal disease treatment and more than half needed restorative work including extractions. This increased level of dental caries in people with CBD indicates the need for better preventive strategies and regular dental visits. This was also reported 10 years later from the same study site (Moosajee *et al.*, 2013).

Oral hygiene is essential but promoting optimal oral hygiene must be underpinned by a sound psychological theoretical base (Michie *et al.*, 2011).

2.6 Supporting optimal oral hygiene

Prevention of oral disease depends on a patient's oral hygiene routine, sugar consumption patterns, use of fluoride and dental attendance (Public Health England, 2014). The benefits of prevention are well recognised. According to Tonetti *et al.*, 2015 facilitation of oral behavioural change is a pre-requisite to implantation of effective oral hygiene. This approach entails individually tailored oral hygiene practices with an incorporated behavioural change technique.

“Behaviour change interventions” can be defined as coordinated sets of activities designed to change specified behaviour patterns” (Michie *et al.*, 2011). However, given the complex nature of behaviour it is important to examine a full range of interventions and the influential factors. A new framework the “behaviour change wheel” (BCW) has been designed recently and it covers a full range of interventions. The BCW entails the design and selection of interventions depending on the nature of the behaviour, identifies the mechanisms that need to be changed in order to change the behaviour, and the interventions that are needed to change those mechanisms (Michie *et al.*, 2011).

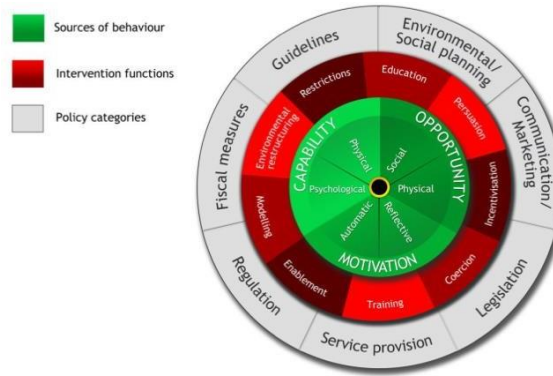


Figure 3 Behaviour Change Wheel (Michie et al., 2011).

Harnacke *et al.*, 2012 demonstrated that when delivering oral hygiene instructions emphasis should be made on correction of missing and neglected areas. Therefore, individualised oral hygiene interventions are more effective in reducing gingival inflammation and bleeding score when comparing to standardised ones.

One approach to behavioural change with facilitation of oral hygiene habits requires Goal setting, Planning and Self-monitoring (GPS) (Newton & Asimakopoulou, 2015). It was also noticed that a patient's perception of benefits of the behavioural change can predict likelihood of their adherence to oral hygiene instructions. GPS is one contemporary approach to support change in oral hygiene behaviour (Newton & Asimakopoulou, 2015). A recent study has demonstrated a positive use of a mobile application "The Brush DJ" to motivate undertaking oral hygiene routine. According to Underwood *et al.*, 2015 70% of those surveyed found that their teeth felt "cleaner", and 90% reported they spent longer when brushing their teeth (Underwood *et al.*, 2015).

2.7 Rationale for the research

The extent of contribution of gingivitis to overall experience of mouth bleeding in people with CBD is unknown, and the proposed research will contribute to this knowledge gap. The research is important, as it is possible that bleeding from the mouth experienced by people with a bleeding disorder may be directly attributable to gingivitis and could be managed effectively through simple oral health advice and timely access to dental care. Clinical dental research suggests that amongst people living with CBDs, bleeding from the mouth was mostly likely to be plaque induced gingivitis, though this was not objectively tested in the reported studies (Moosajee *et al.*, 2013; Rafique *et al.*, 2013). It was also noted that amongst people with CBD oral health literacy was low and access to dental care was poor thus significantly reducing opportunities to correct misinformation (Fiske *et al.*, 2002; Kalsi *et al.*, 2012). Patients living with a CBD were reported to stop brushing their teeth in the presence of blood. They attributed the bleeding to their bleeding disorder, rather than to the presence of dental plaque and gingivitis (Hitchings, 2012).

There is little understanding of people living with vWD's knowledge, beliefs, impact and experience of bleeding gums. In addition, the association between dental plaque induced gingivitis and objective markers of vWD levels in people living with vWD has not been estimated previously. The proposed research will address this knowledge gap in a cohort of patients living with vWD. This information can be then used to form interventions to promote self-care (particularly oral hygiene), in people living with CBD.

The present study is part 1 (baseline data set) of a Randomised control trial (RCT) which is currently recruiting and aims to examine the effectiveness of PMR and OHI versus OHI alone in management of gingivitis in people with vWD.

2.8 Aims of the study

The aims of the study were to describe the presence and impact of bleeding from the mouth in people living with vWD and explore the association between plaque induced gingivitis and objective measures of vWD.

Chapter Three: Materials and methods

3.1 Research aims

The aims of the study were a) to describe the presence and impact of bleeding from the mouth in people living with vWD and b) to explore the association between self-report of bleeding gums, plaque induced gingivitis and objective measures of vWD.

It was hypothesised that the bleeding from the mouth reported by participants (self-report) would be associated with objective measures of levels of plaque and severity of gingivitis in the mouth and would have no association with their bleeding disorder as measured through objective measures of the vWD. In other words, bleeding gums in people living with vWD was hypothesised to be largely attributable to presence of plaque and gingivitis.

In order to fulfil the study aims, the following study objectives were set:

1. To describe the perception of health, oral health, OHRQoL and dental behaviours amongst people living with vWD
2. To describe the extent of self-report of bleeding gums including timing and attribution amongst people living with vWD
3. To record the extent of plaque accumulation and gingival bleeding using clinically objective measures amongst people living with vWD
4. To record objective markers of vWD in people living with vWD
5. To assess the relationship between subjective and objective measures of bleeding from the mouth.

3.2 Methods

3.2.1 Participants

3.2.1.1 Study design

The present study is cross sectional and forms the baseline data set for a two-armed randomised controlled trial with the same group of patients exploring whether professional mechanical plaque removal (PMPR) plus oral hygiene instruction (OHI) is superior to (OHI) alone in improving gingival outcomes.

3.2.1.2 Setting

The study was carried in the National Coagulation Centre (NCC), at St James's Hospital, Dublin, Ireland. NCC provides a range of services for people with bleeding and clotting disorders. These include inpatient and outpatient services delivering comprehensive care. According to the 2018 St James's annual report, the Haematology Department treated 6,261 individuals in 2017 (St James's Hospital, 2018). All Irish patients with vWD are registered on a national database retained in the NCC. Patients attending for yearly reviews were approached and recruited from those appointed at the NCC for annual clinical reviews from February 2018 till 4th March 2019.

3.2.1.3 Inclusion criteria

To be included in the study participants had to be:

- 18 years or older on the day of approach
- able to provide informed consent after reading a participant information sheet.

- have a Basic periodontal examination (BPE) * score of 2 or below on the day of recruitment.

3.2.1.4 Exclusion criteria

Participants were excluded from the study if any of the following criteria or conditions were present:

- patients aged < 18 years old,
- pregnant women, because it is known that they will have increased gingival inflammation; elevated capillary permeability and gingival exudate (Gursoy *et al.*, 2013);
- current smokers, because of impairment in vascular gingival microcirculation and immune systems of individuals (Albandar, 2002);
- people living with diabetes, because significantly higher gingival bleeding, exaggerated inflammatory responses and higher prevalence of inflammatory cytokines are seen in diabetic patients when compared to non-diabetic patients (Albandar, 2002);
- individuals who had been prescribed antibiotics within the last six weeks on the day of recruitment, because these could potentially offer an additional benefit to the periodontium (Kapoor *et al.*, 2012);
- adults with acute mental health problems, dementia and intellectual disabilities, because they were unable to consent themselves due to inability to retain information and weigh risks and benefits;
- patients with a history of inhibitor development to vWF;
- a BPE score greater than 2.

3.2.2 Approach and recruitment

When attending their annual review patients were asked by a gatekeeper if they were interested to participate in a dental study. Patients were supplied with a Patient Information Leaflet (Appendix 1) (PIL). If interested they were put on a list and then after at least 24 hours phoned by the research dental nurse (LP) with the appointment to attend the dental clinic on a scheduled Thursday dental clinic. On the day of the appointment a spare copy of the PIL was available and a consent form (Appendix 2) was signed. All participants were informed that they would not derive any direct benefit from participation in the study, however all would receive a complimentary tooth debridement. It was emphasised that patient participation was entirely voluntary and would not affect their usual care in St James Hospital. This approach gave patients at least 24 hours to consider participation.

3.2.2.1 Informed Consent

On the day of their annual review appointment the patient was seen by their lead haematologist clinician and asked if they wished to be introduced to the dental team to participate in the research. This was done to avoid pressure to participate. There was an opportunity for participants to further discuss the study, assess what participation involved and have questions answered before signing consent.

Written informed consent was then sought from participants. Their consent forms were collected by LP and kept in a locked office. Each participant was then given a unique identifier code to allow data to be anonymised.

3.2.3 Baseline questionnaire

All patients recruited to the study were asked to complete a baseline questionnaire (Appendix 3) investigating self-report of oral health, oral health related quality of life, behaviours and dental anxiety, perception and experience of gingival bleeding (Wienman & Petrie, 1996; Slade & Spencer, 1994; Nutall *et al.*, 2011). The items used were drawn from the work of Wienman & Petrie, 1996; Slade & Spencer, 1994; Nutall *et al.*, 2011; Humphris *et al.*, 1995; Mohd *et al.*, 2017, but some specific questions pertinent to this study were developed, specifically to time at which bleeding stopped after performing oral hygiene.

The questionnaire items on perception of bleeding had been used previously in a study by Mohd *et al.*, 2017, which had investigated beliefs and behaviours amongst people with CBD. The version used in this study was piloted and found to take 15 minutes to complete. None of those on whom it was piloted reported any difficulty with understanding the questions.

The anonymised questionnaire was administered and collected by the principal investigator (SA). The data collected in the questionnaire was used as a baseline to assess change once the RCT was completed.

3.2.3.1 *Gingival and plaque level assessment*

Participants were then introduced to Dr Alison Dougall (AD) the research dentist who briefly reviewed the study inclusion and exclusion criteria with participants. All participants received an assessment of the gingivae using the BPE (BSP, 2016) for inclusion/ exclusion purposes. Only those scoring 2 or below were eligible to participate.

BPE was carried out using the WHO probe with a probing force 20-25 gm and walked around the buccal, labial, lingual and palatal surfaces, excluding third molars (BSP, 2016). The teeth and mouth were divided in 6 sextants.

17-14	13-23	24-27
47-44	43-33	34-37

Table 3 BPE Sextant division

Only the highest score of all the teeth in each sextant was recorded.

Any patient scoring 3 or above in the BPE was not eligible to take part in the intervention. Codes 3 and 4 indicate probing depth of > 3.5 mm and therefore required more detailed periodontal charting and treatment. These patients were offered a course of treatment with dental hygiene students to manage their periodontal condition. Restorative dental care (fillings, crowns and bridges) were not offered to any participant as this dental treatment could be provided routinely in a general dental practice setting by their GDP and was not part of the study. This was explained previously in the participant information sheet. AD then performed on eligible recruited participants a recording of the Modified Papillary Bleeding Index (MPBI) (Burnett *et al.*, (1980)), Gingival Index (GI) (Loe & Silness, 1963) and Quigley Hein Index modified (QHIM) by Turesky *et al.*, 1970. These will be discussed later under study outcome assessment. Plaque was disclosed according to the Quigley Hein Index modified (QHIM) by Turesky *et al.*, 1970. The participant was told their plaque score. Eligible participants were assigned to a control or intervention group using a random number sequence. Sealed

envelopes were used to allow allocation concealment. AD was blind to a later group allocation.

3.2.3.2 *Standardised oral hygiene instruction (OHI)*

All participants then received a standardised ten minute oral hygiene instruction by SA. The plaque score was explained to the patients, and they were advised on causes of gingival bleeding and how to best manage their oral hygiene. A standard text was used for all patients (Appendix 4). The participants were given an oral home pack care and leaflet (Appendix 5), an oral hygiene chart (Appendix 6) and a link for downloading an app if they wished to do so. All materials were evidence based (Conforti *et al.*, 2003; Harnacke *et al.*, 2012; Irish Oral Health Services Guideline Initiative, 2008; Loe *et al.*, 1965; Lee *et al.*, 2007; Mitchell *et al.*, 2012; Public Health England, 2014; Sambunjak *et al.*, 2011; Slot *et al.*, 2008) and were reviewed for suitability for people with CBD. The OHI was personalised (based on their plaque score and disclosed plaque accumulation sites), and used planning and goal setting principles to tailor the advice to the needs of the individual (Renz *et al.*, 2007, Renz & Newton, 2009, Suresh *et al.*, 2015, Asimakopoulou & Newton 2015).

3.2.4 Outcome measures

3.2.4.1 *Non-clinical outcome measures*

The questionnaire (Appendix 3) was developed from a battery of tools and items exploring knowledge, beliefs around bleeding gums and behaviours (including dental anxiety) around tooth brushing and dental attendance. These data enabled the first two study objectives to be achieved:

1. Perception of health, oral health and OHRQoL and dental behaviours in people with vWD
2. Self-report of bleeding from the mouth including timing and attribution in PWD

Self-report of oral health (White *et al.*, 2012) is a global self-rating and enables individuals to give an overall summary of their oral health. It is important when assessing change and interpreting oral health related quality of life scores. Oral health related quality of life questions by Slade & Spencer (1994) were included to assess the impact of oral disease on individuals, their level of disability and any discomfort associated with the mouth, teeth or dentures. The time period was set at “in the previous 12 months”.

Behaviour and dental anxiety questions assessed participant’s attitude and beliefs about their oral health and dental care. These would be used to inform the OHI intervention in the RCT and to increase adherence to oral hygiene using self-monitoring (diary and a leaflet) and goal setting (Newtown & Asimakopoulou, 2015). They were also collected to give context to possible barriers to accessing dental care in the study group.

Dental anxiety level was assessed using the Modified Dental Anxiety Scale (Humphris *et al.*, 1995) which included questions that examine aspects of dental treatment that initiate anxiety in dentally anxious individuals.

The Illness perception questionnaire (IPQ) by Wienman & Petrie (2011) assessed patients experience and understanding about their bleeding gums. These IPQ items had been adapted and modified to study bleeding gums in CBD in a

previous study by Mohd *et al.*, 2017. In the present study these items were used to assess beliefs and control beliefs in relation to bleeding gums. Participants were also asked to provide their own attribution as to the cause of bleeding gums.

3.2.4.2 *Clinical outcome measures*

The objective clinical outcome measures were used to enable achievement of objectives, 3, 4 and 5 of the study. Plaque was disclosed and levels of plaque assessed with the Quigley Hein Index (modified) (Turesky *et al.*, 1970). Gingival bleeding was assessed using a partial scoring objective method the Gingival Index (Loe & Silness, 1963). This index has been used widely and has been shown to be acceptable and easily reproducible for research purposes. It was designed for the visual assessment of the gingivae and to record qualitative changes in the gingivae. As this study and the RCT was specifically about bleeding, spontaneous bleeding and the response of the gums to tooth brushing and flossing an index was chosen which would be sensitive to assessing change in gingivae. The Modified Papillary Bleeding index (MPBI) (Rebelo & De Queiroz, 2011) was chosen because it fulfilled the latter requirements and measured the timing of bleeding, differentiating between spontaneous bleeding and delayed.

The sequence of the recording was that the GI was recorded first, followed by MPBI and then the Quigley Hein Index (modified) to assess levels of plaque.

GI (Loe & Silness, 1963)

The GI was scored with a blunt probe at 45° angle on the buccal, mesial, lingual and distal surfaces. Mesial and distal scores were determined at a point midway between the line angle and the col area.

- Score 0 Normal gingiva
- Score 1 Mild inflammation slight change in colour, slight oedema; no bleeding on probing
- Score 2 Moderate inflammation redness, oedema, glazing; bleeding on probing
- Score 3 Severe inflammation marked redness and oedema, ulceration; tendency toward spontaneous bleeding

GI= Total Score/ number of surfaces examined

The results were interpreted as following:

0.1-1 Mild gingivitis

1.1-2 Moderate gingivitis

2.1-3 Severe gingivitis

MPBI (Burnett *et al.*, 1980)

MPBI was scored with a blunt probe at the mesial line angle of the tooth surface and carefully swept forward into the mesial papilla. Teeth were assessed from the second molar to the lateral incisor. Indices were derived from the buccal areas of maxillary left and mandibular right, and the lingual areas of maxillary right and mandibular left. The appearance of bleeding was timed as:

0 - no bleeding within 30 s of probing;

1 – bleeding between 3 and 30 s of probing;

2 - bleeding within 2 s of probing;

3 – bleeding immediately upon probe placement.

Total score of MPBI was recorded as was the worst score per patient.

Both GI and MPBI were explained to the patients and recorded on the leaflet and daily brushing chart for their motivation.

Quigley Hein Index (modified) (Tureskey *et al.*, 1970)

The last stage of clinical assessment was to record to assess levels of plaque. This was carried out by Dr Dougall. Data were entered on the chart provided. Disclosing agent was applied on non-restored tooth surface. QHI was assigned to each buccal and lingual non-restored surface of all the teeth except third molars.

To find Index = Total score ÷ Number of surfaces examined

- Scores 0 No plaque
- Score 1 Separate flecks of plaque at the cervical margin of the tooth
- Score 2 A thin continuous band of plaque (up to one mm) at the cervical margin of the tooth
- Score 3 A band of plaque wider than one mm but covering less than one-third of the crown of the tooth
- Score 4 Plaque covering at least one-third but less than two-thirds of the crown of the tooth
- Score 5 Plaque covering two-thirds or more of the crown of the tooth

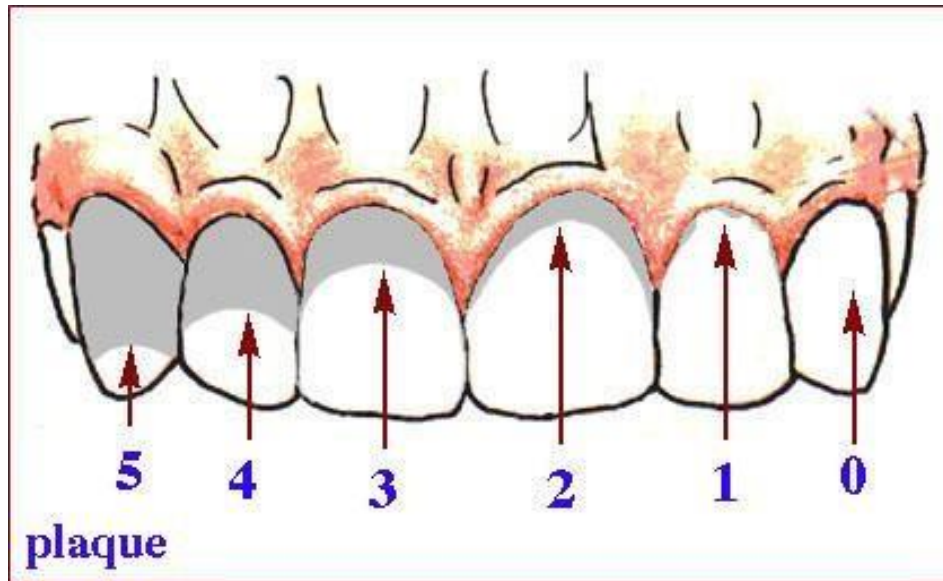


Figure 4 Tureskey et al., 1970

Score Interpretation:

0-1 is considered low

≥ 2 is considered high

The plaque score was demonstrated, written down and explained to the patients. Individuals were advised on plaque- induced gingival inflammation and bleeding. It was used as a motivational tool in improving their home care and how to best manage their oral hygiene (3.2 above).

3.3 Sample size

Statistical advice was obtained during preparation of the outline study protocol and sample size calculation was sought from a statistician, Dr Erica Donnelly-Swift. This sample size calculation was based on the accompanying RCT intervention study which is not reported upon in this thesis. However, the baseline data recorded for that RCT provide the data reported upon in the present study.

3.4 vWD markers

To assess vWD levels, blood markers of vWD Ag and vWD Rco were extracted from the patient record by the direct care team (LP) and shared anonymously with the principal researcher (SA). In this study many of the participants were classified as having low vWF (between 30-50dg/l)

3.5 Data analyses

The data analyses were planned as followed:

The description of participants in the total sample and subgroups were to be presented using simple descriptive statistics. Self-report of oral health, oral health related quality of life (OHIP-14) at the threshold of “occasional and above”, self-report of dental behaviours, dental anxiety MDAS score, perception, experience and frequency of gingival bleeding, MPBI, GI, PI were reported as means and standard deviation (SD) or medians and interquartile differences as appropriate. Frequency and relative frequency distribution were also reported for the data.

3.6 Ethics and good clinical practice (GCP)

This study was approved by Tallaght Hospital Research Ethics Committee and was granted in September 2017. The research team included Ms Sviatlana Anishchuk (SA), Prof Blanaid Daly (BD), Dr Alison Dougall (AD) and Ms Laura Parkinson. (LP). All underwent good clinical practice (GCP) training at St James Hospital prior to commencement of the study.

Chapter Four: Results

4.1 Introduction

This study recorded a baseline dataset which was part of a larger RCT study assessing the effectiveness of oral hygiene instruction (OHI) versus professional mechanical plaque removal (PMPR) plus oral hygiene to improve gingival outcomes.

The baseline study recorded self-report of health and oral health, oral health related quality of life, oral health behaviors, dental anxiety, perception and experience of gingival bleeding. These data were supplemented by objective clinical data assessing gingival health and levels of vWD factor. A full description of the dataset recording system is found in Appendix 7. With these data it was possible to produce results to address the study objectives.

4.2 Participants and setting

A power calculation indicated that a sample of N=56 individuals with vWD was required to sufficiently power the main RCT. Patients who were attending for their annual review in the OPD clinic and meeting the study inclusion criteria were approached and invited to participate in the research. Up until to the 4th March 2019 thirty individuals agreed to participate but a full data set was only available for n = 24. Recruitment for the RCT was planned to continue after the 4th March 2019, but this was outside the cut off period for the submission timeline for the MSc (TCD) of the 21th March 2019. A sample of N=24 was achieved up to that date (43% achieved sample) and the results presented here reflect that number.

The data for the present study were gathered between the 17th May 2018 and the 4th March 2019. Recruitment is ongoing for the RCT.

All data were recorded on two separate Excel spreadsheets. The self-report data and clinical data were entered by SA, and every 10th entry was checked for entry accuracy. Patient data were extracted from the patient record by a research nurse (Laura Parkinson, LP) who was a member of the direct care team. She fully anonymised the data set and entered clinical markers for vWD (vWF AG and Rco). Data entry was checked for every 10th entry. Each record took approximately five minutes to input.

SA then merged the data into one Excel spreadsheet and inputted the data into SPSS version 24. The data were then cleaned and checked again for any anomalies. The statistical analyses were conducted in two phases:

1. Descriptive and summary analyses for each variable
2. Bivariate analyses assessing the association between gingival health (GI), MBPI and plaque levels and i) self-perception of bleeding ii) clinical markers for vWD (vWF AG and Rco)

4.3 Gender and age distribution

All participants in this report of the baseline data (N=24) declared their gender, the sample was predominantly female (88 %; n=21) and there were three men (12%).

The age of participants ranged from 19 to 75 years. Figure 5 illustrates the age distribution amongst all participants. The mean age for all participants was 42.0 (SD 17.0), for women this was 40.0 years (SD16.4) and for men this was older at 56 SD 17.4.

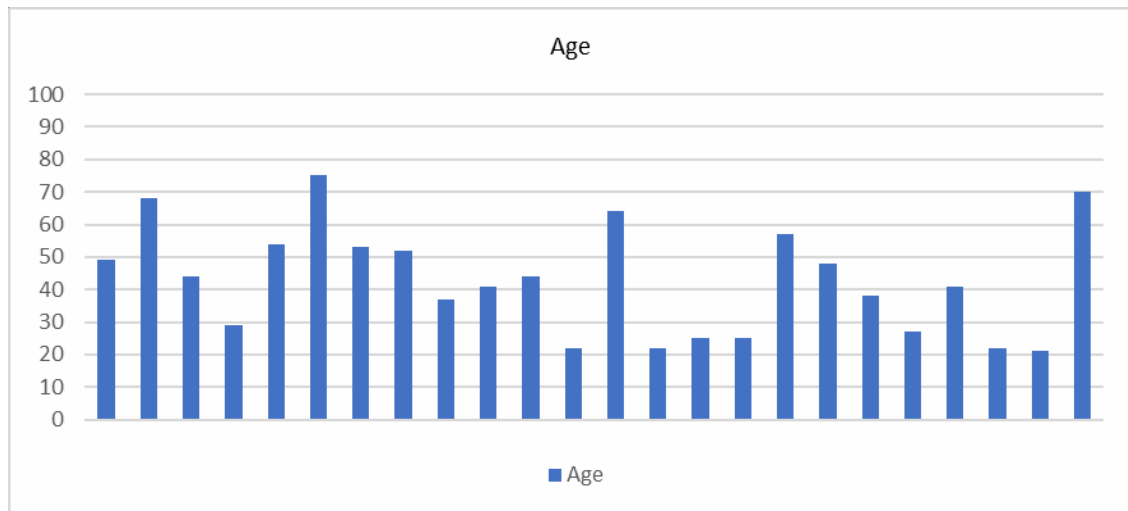


Figure 5 Age distribution of participants N = 24

4.4 Baseline questionnaire

At the initial visit participants were asked to complete a baseline questionnaire investigating their self-rated health and oral health, oral health related quality of life, oral health related behaviours and dental anxiety, perception of bleeding gums and experience of gingival bleeding. This questionnaire was composed of fourteen questions and sub questions that were previously validated for use amongst people with CBDs (Appendix 3).

4.4.1 Self rating of health and oral health

Most participants (92%; n=22) rated their general health as “good” and “very good”. While 71% (n=17) rated their oral health as “very good” and “good, though 19% (n=7) described their oral health as “fair”. Figure 6 presents the breakdown of self-rating of health and oral health.

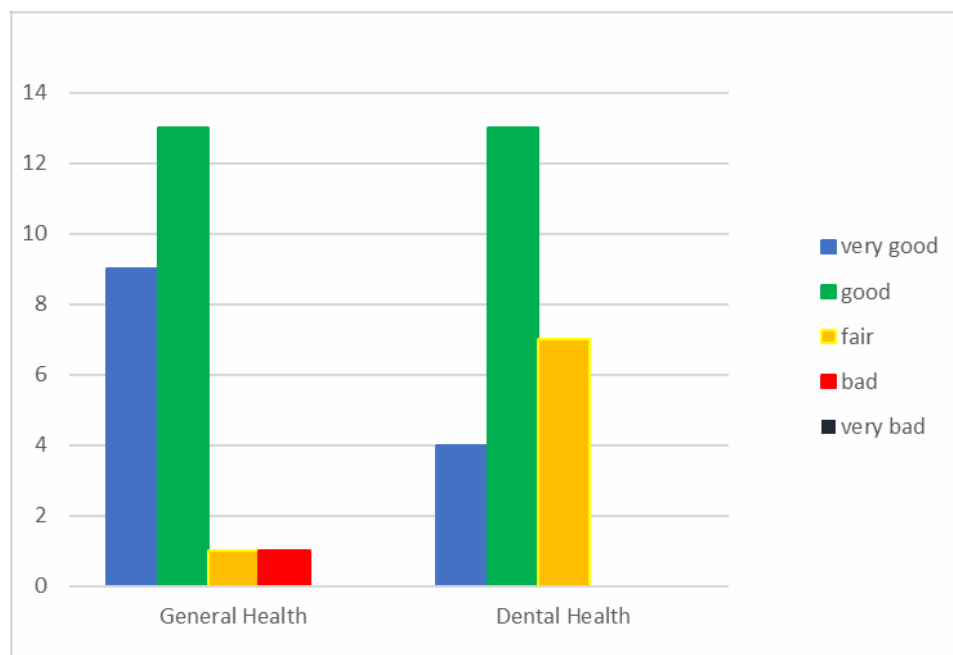


Figure 6 Self rating of health and oral health N=24

4.4.2 Oral health related quality of life (OHIP14) in the last 12 months

Oral health related quality of life assesses the impact of oral health on quality of life. The shortened format OHIP-14 assesses 7 domains (functional limitations, psychological discomfort, pain, physical, psychological and social disability and handicap) using 14 questions. Participants rate the frequency of impact from never (1) to very often (5). OHIP -14 may be presented either as a total score (ADD score), or as a mean score which reports the number of impacts experienced by an individual at a threshold. In the present study the researcher

used the threshold of problems that were experienced at least occasionally, often and very often. Table 4 presents the data for OHIP 14 total score and OHIP-14 mean score.

	Total OHIP14 ADD Score	Total mean OHIP14
Mean SD	23.8	3.2
Median	21.5	2
Mode	15.0	2
Minimum-Maximum	14-43	0-11

Table 4 Measures of central tendency for the mean OHIP score at the threshold of occasional, often and very often

Figure 7 shows the relative frequency of oral impacts experienced by the sample. Only 20% (n=5) of the sample reported no impact on quality of life.

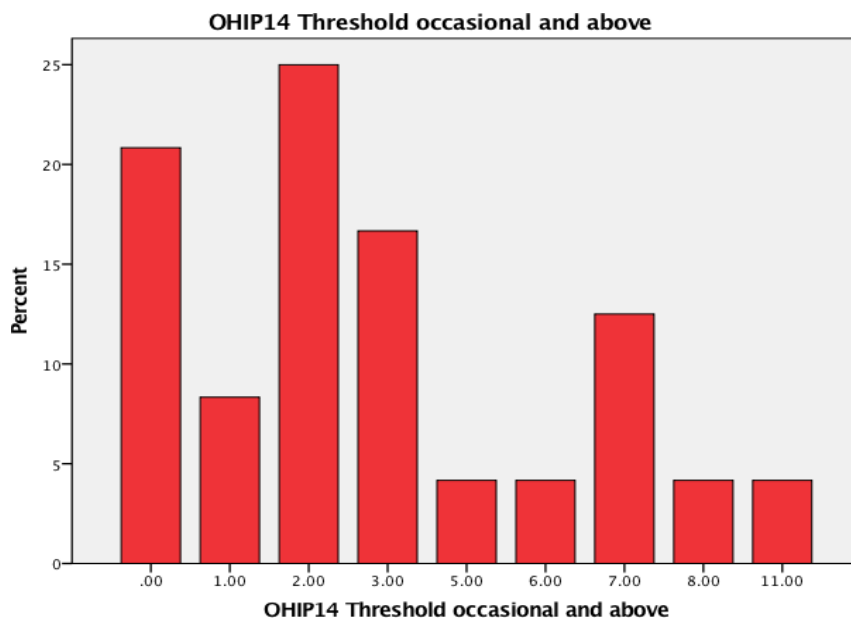


Figure 7 Relative frequency OHIP Threshold occasional and above N = 24

Problems with “teeth, mouth and gums” (Slade, 1997)	Number of people and proportion of sample affected			All affected n; %
	Occasionally n;%	Often n;%	Very Often n;%	
Trouble pronouncing words	5 (21%)	-	-	5 (21%)
Felt sense of taste worsened	1 (4%)	1 (4%)	-	2 (8%)
Had a painful aching in the mouth	7 (29%)	3 (13%)	-	10 (42%)
Found it uncomfortable to eat any food	7 (29%)	2 (8%)	-	9 (37.5%)
Have been self conscious	5 (21%)	2 (8%)	-	7 (29%)
Felt tense	8 (33%)	1 (4%)	-	9 (37.5%)
Had an unsatisfactory diet	5 (21%)	-	-	5 (21%)
Had to interrupt meals	4 (17%)	-	-	4 (17%)
Found it difficult to relax	9 (37.5%)	1 (4%)	-	10 (42%)
Have been a bit embarrassed	4 (17%)	-	-	4 (17%)
Have been irritable with other people	4 (17%)	-	1(4%)	5 (21%)
Had difficulty doing usual jobs	1 (4%)	1 (4%)	-	2 (8%)
Life in general was less satisfying	3 (13%)	-	-	3 (13%)
Have been totally unable to function	2 (8%)	-	-	2 (8%)

Table 5 The breakdown of OHIP-14 for each item by threshold N = 24

4.4.3 Attribution of oral condition to impact on OHRQoL

Participants were asked to self-report the oral condition most often impacting the quality of life. The most frequent response that affected people’s quality of life was “toothache” and it was experienced by 63% (n=15) of people. Half of the

participants suffered from sensitivity (50%; n=12) and 33% (n=8) reported their quality of life was negatively impacted due to bleeding gums. The other conditions which were reported less commonly are illustrated in Figure 8 below.

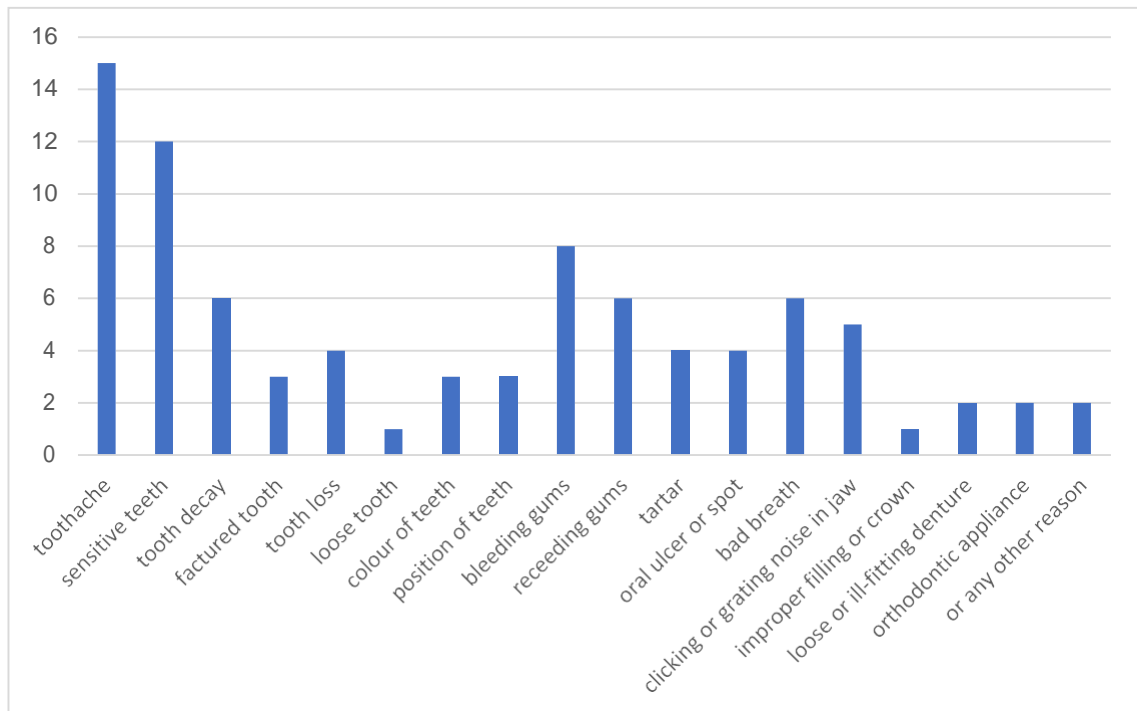


Figure 8 Frequency distribution of oral conditions impacting on OHRQoL

4.4.4 Behaviours

4.4.4.1 Smoking

From those surveyed, all 24 answered the question and 54% (n=13) said they had never smoked in their life, while the remainder 46% (n=11) have tried or previously smoked but quit.

4.4.4.2 Consumption of sugary drinks N = 24

Twenty-four participants answered questions on their consumption of sugary drinks. Almost half of the participants 46% (n=11) responded “rarely or never” to the intake of fizzy drinks, fruit juice or soft drinks, excluding sugar-free drinks. While one quarter of participants (25%; n=6) reported they have sugary drinks 1-2 times a week and the rest (29%; n=7) reported having sugary drinks between 3-5 times a week (Figure 9). Figure 10 below presents the frequency of sugar intake in hot drinks (e.g.: tea, coffee) amongst participants.

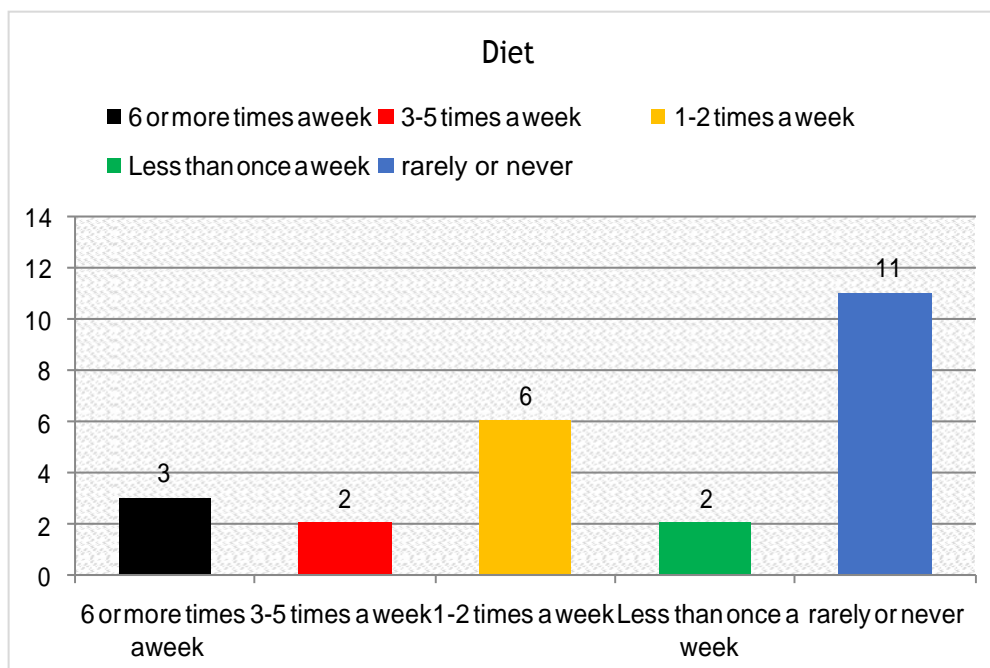


Figure 9 Frequency of sugar intake amongst participants N = 24



Figure 10 Addition of sugar to hot drinks reported by participants N = 24

4.4.4.3 Dry mouth

Only a small number of individuals (13%; n=3) reported they had dry mouth “fairly often”. Those that answered occasionally, 38 %, (n=9) said they drank water in order to relieve dry mouth. See Figure 11.



Figure 11 Frequency of dry mouth N = 24 participants

4.4.4.4 Teeth and Denture Cleaning

Participants were asked about their brushing and interdental cleaning habits and all 24 people responded. The majority 67% (n=16), of people reported they brushed their teeth twice daily. Slightly over one fifth (21%; n=5) cleaned their teeth more than twice a day and the rest reported cleaning once a day. Only one of the participants was wearing a removable prosthesis (dentures). All those surveyed said they had a toothbrush and a toothpaste in their possession. The majority (88%; n=21) responded to say they used additional aids when cleaning, such as using mouthwash (71%; n=17), dental floss (46%; n=11), electric toothbrush (42%; n=10), sugar free chewing gum (29%; n=7), interdental/ toothpicks/ woodsticks (25%; n=6) and interspace brushes (8%; n=2). There were various toothpaste brands used: Oral B, Sensodyne, Colgate, Elgidium, CB12.

All were fluoridated. The bar chart below (Figure 12) illustrates the variety of cleaning aids used at the time of the initial visit.

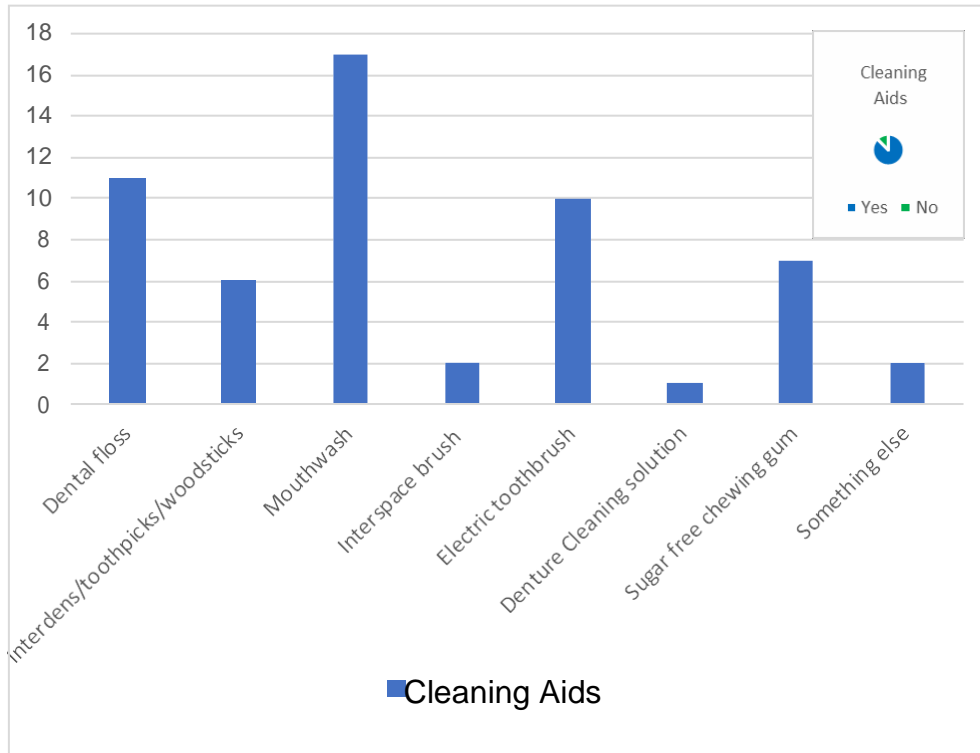


Figure 12 Cleaning aids used by participants N = 24

4.4.4.5 Denture use

One participant reported that he used a denture.

4.4.4.6 Dental Attendance patterns

Over half of the 24 participants (58%; n=14) responding reported that if they went to a dentist tomorrow, they would require dental treatment, for instance fillings, cleaning and dentures. More than half of those responding (63%; n=15) said they went regularly for a check up and at least once every six months and had recently attended within the last 6 months (55%; n=12). A quarter of those responding described themselves as an “occasional” attender (25%; n=6). Some went at

least once every year (29%; n=7) and had attended within the last 7-12 months (25%; n=6). Those responding said their last dental visits were associated with a routine check-up (63%; n=15), emergency/ urgent treatment (17%; n=4) or other treatment (17%; n=4) respectively.

One sixth (17%; n=4) said they only went to see a dentist when having trouble with their teeth/dentures. The same number reported visiting their dentist less frequently than every two years but not longer than five years (17%, n=4). One person said he/she went to see the dentist at least once every two years. Figure 13 presents a breakdown of the data.

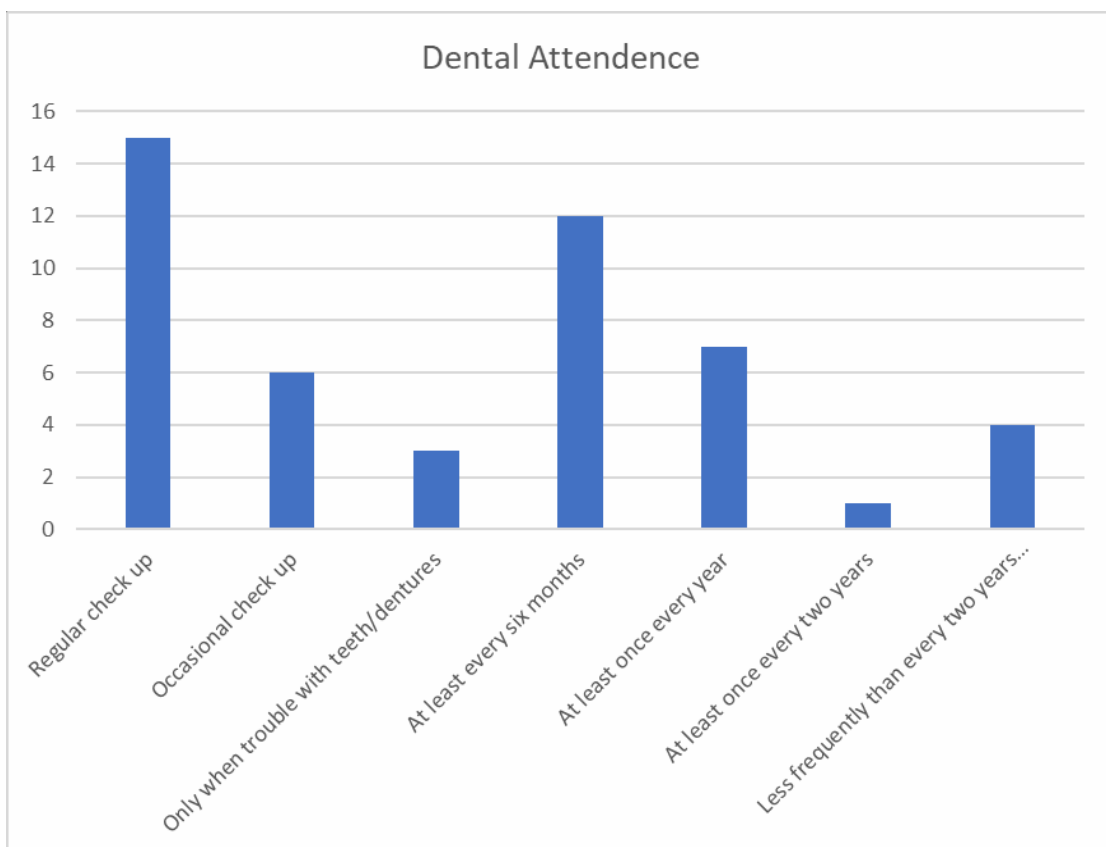


Figure 13 Dental attendance pattern for participants N = 24

The following responses were given for reasons for not visiting the dentist: don't need to go/ nothing is wrong with teeth (n=3), afraid to go to the dentist (n =2), keep forgetting/haven't had a chance to go (n =2), can't afford the charges (n=1), confused about vWD (n=1), had orthodontic treatment (n=1) and did not need to see a "dentist", dentist did not come back with appointment (n=1) and "just don't think about it until it hurts" (n=1), "when the tooth was taken out was very sore afterwards" (n=1).

Overall, of those surveyed most were happy with the dental care they received (71%; n=17), a small number was not sure (8%; n=2) and some felt that the care could have been better (17%; n= 4) (Figure 14).

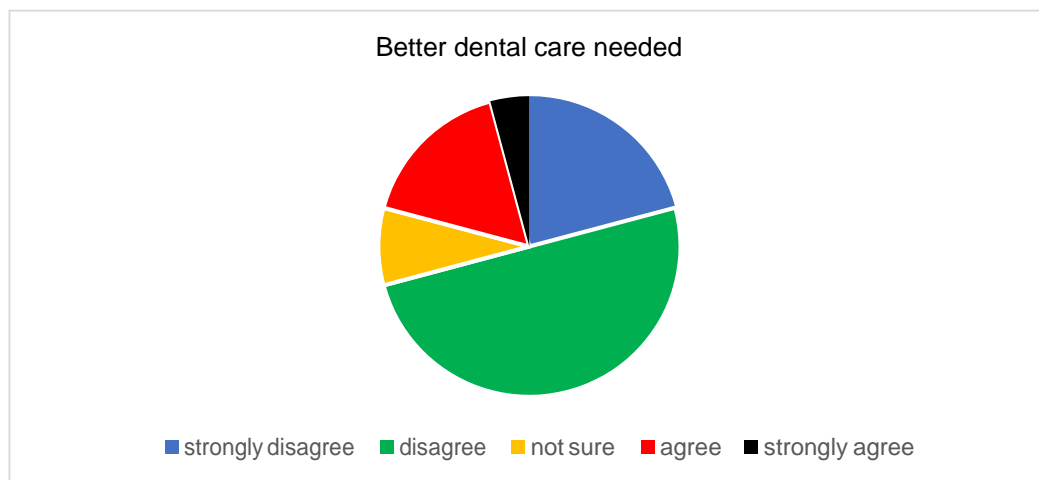


Figure 14 Response to rating of dental care received N = 24

4.4.5 Dental anxiety scale (MDAS)

The MDAS scale contains five items, with each item rated from 1 (not anxious) to 5 (extremely anxious). Maximum available scores were from 5 to 25. Of those surveyed, the maximum score was 22 and the minimum score was 5. The mean

MDAS score was 10.4 SD 5.4. Cut offs for anxiety had been identified as mild (5-9), moderate (10-18) and severe (>19) (Humphris *et al.*, 1995). Figures 15 and 16 present the breakdown for dental anxiety by item and by level of anxiety.

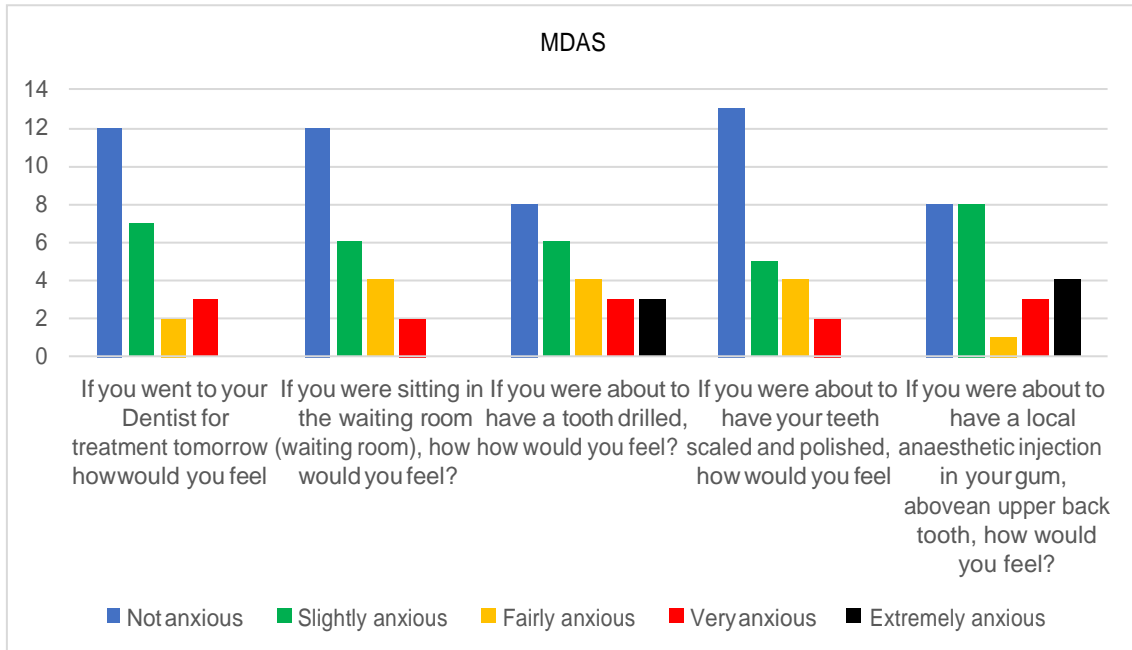


Figure 15 MDAS response scale by level of anxiety N = 24

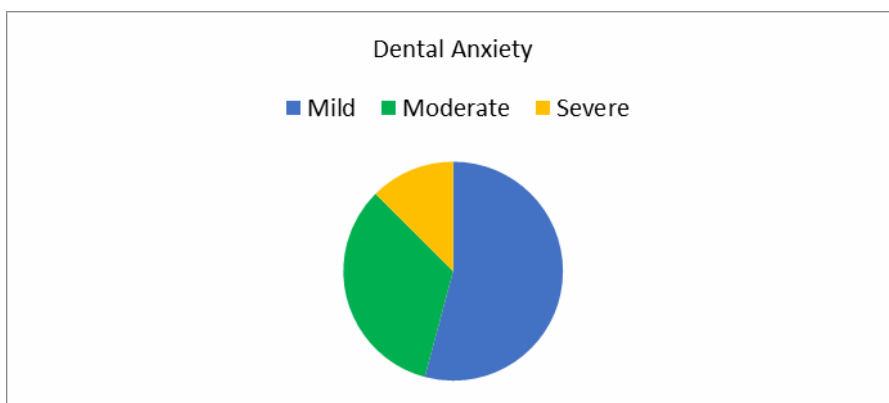


Figure 16 Dental anxiety distribution amongst sample N = 24

4.4.6 Experience of gingival bleeding

Participants were asked to rate their experience of gingival bleeding from 1 (never) to 10 (very often), with 5 defined as the midpoint between the two extremes. See distribution Figures 17, 18, 19 and 20. Almost two thirds of respondents did report bleeding gums at the frequent end of the scale (mean 5.1 SD 2.5). When answering if this bleeding occurred spontaneously most responded “never” or “almost never” with a mean score of 2.5 SD 2.1. There was a range of responses to the question “Do your gums bleed when you brush your teeth and/ or floss your teeth?” most people reporting frequent gum bleeding (mean 5.5 SD 2.8). When asked about the timing that was involved in stopping the bleeding after tooth brushing/flossing the mean response was 3.4 minutes and SD 2.0. Sixty-seven per cent (n=16) of respondents said bleeding stopped in less than five minutes and 17% (n=4) between 5 to 10 minutes.

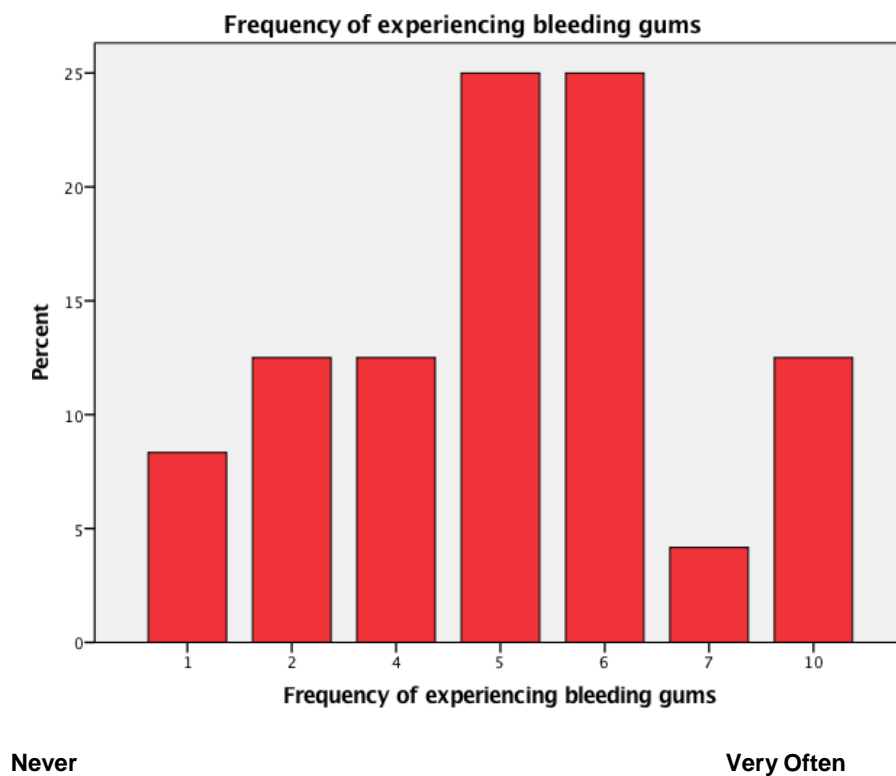


Figure 17 Relative frequency of experiencing bleeding gums N = 24 mean 5.1 (SD .2.5)

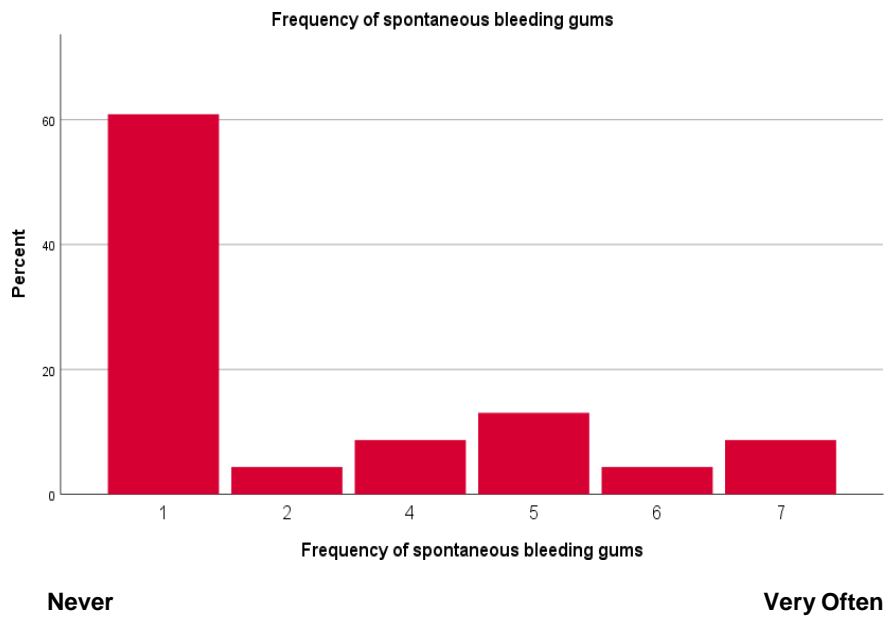


Figure 18 Relative frequency of spontaneous bleeding gums $N = 24$ mean 2.5 (SD 2.1)

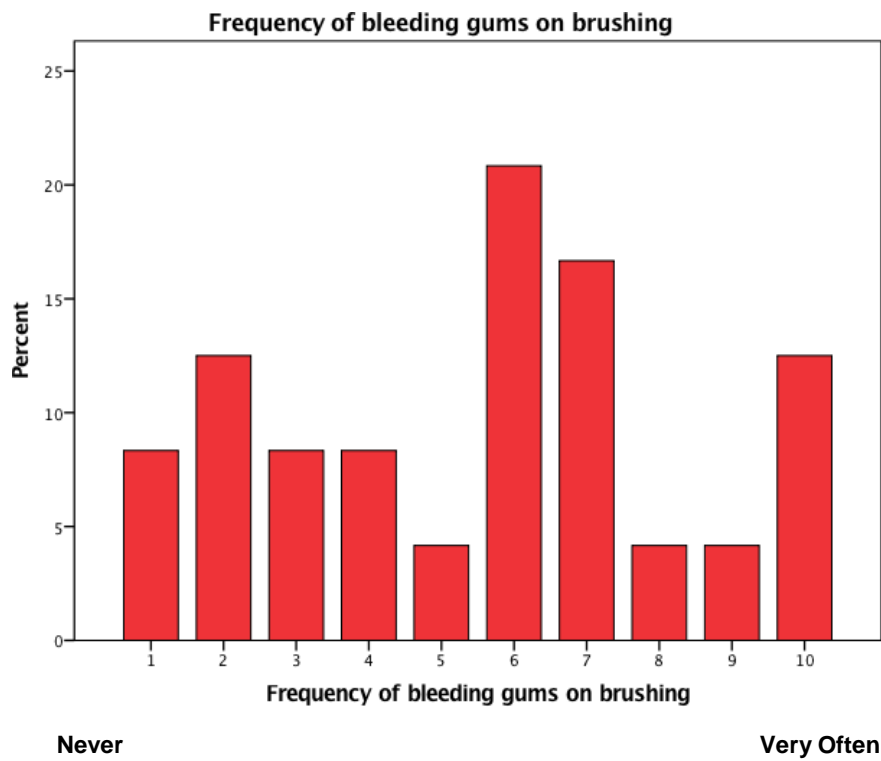


Figure 19 Relative frequency of bleeding gums on brushing/ flossing $N = 24$ mean 5.5 (SD 2.8)

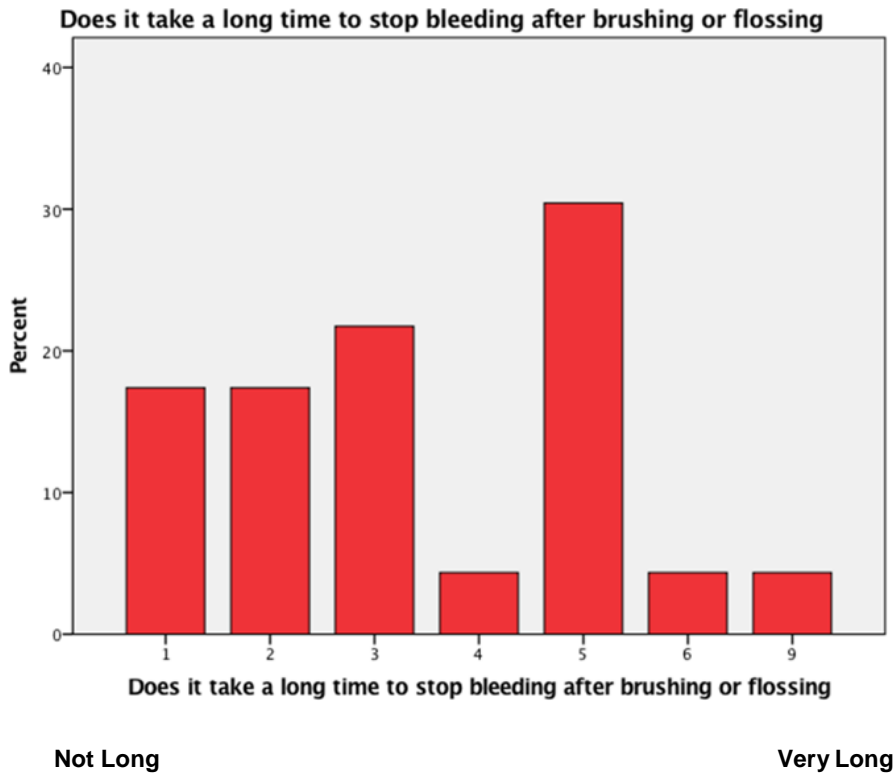


Figure 20 "Does it take a long time to stop bleeding after brushing or flossing?" N= 24 mean 3.4 (SD 2.0)

4.4.7 Perception of bleeding questionnaire (IPQ)

Half of the participants did not feel that their bleeding gums had affected their life (50%; n=12) or affected them emotionally (46%; n=11). There was a range of responses to the question 'How much control do you feel you have over bleeding gums?' with the majority indicating they did not feel as if they had control over their bleeding gums, yet the mean response (5.1) reported for 'How much do you think treatment can help bleeding gums?' suggested that participants felt that dental treatment would help their bleeding gums. See distribution Figures 21, 22, 23, 24, 25, 26 and 27 for more details.

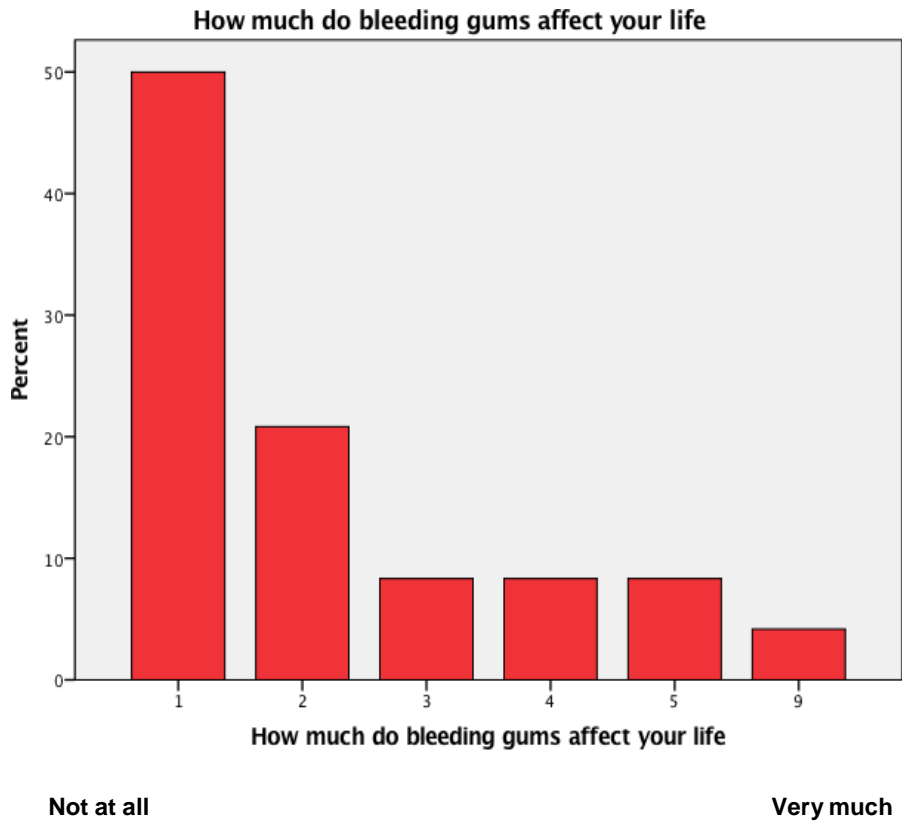


Figure 21 "How much do bleeding gums affect your life?" N = 24 mean 2.3 (SD 2)

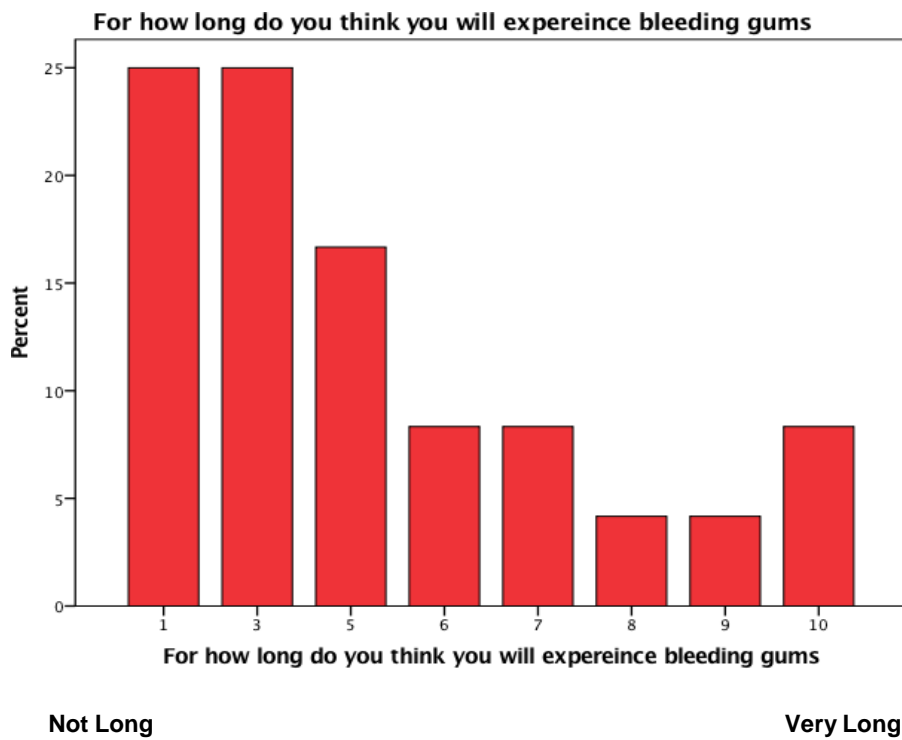


Figure 22 "For how long you think you will experience bleeding gums?" N = 24 mean 4.6 (SD 3)

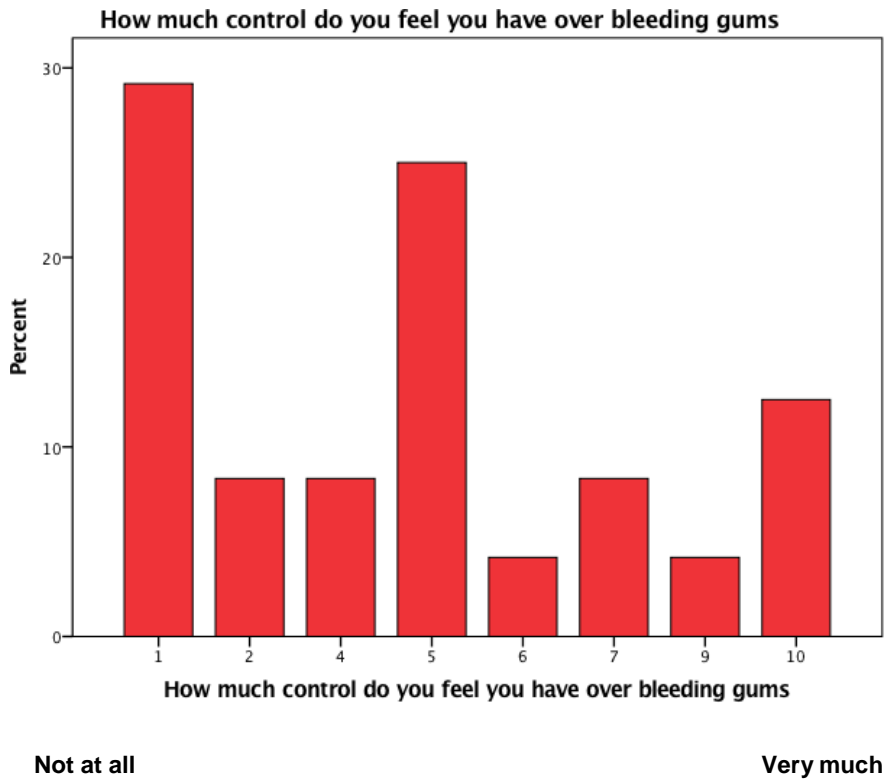


Figure 23 "How much control do you feel you have over bleeding gums?" N =24 mean 4.5 (SD 3.1)

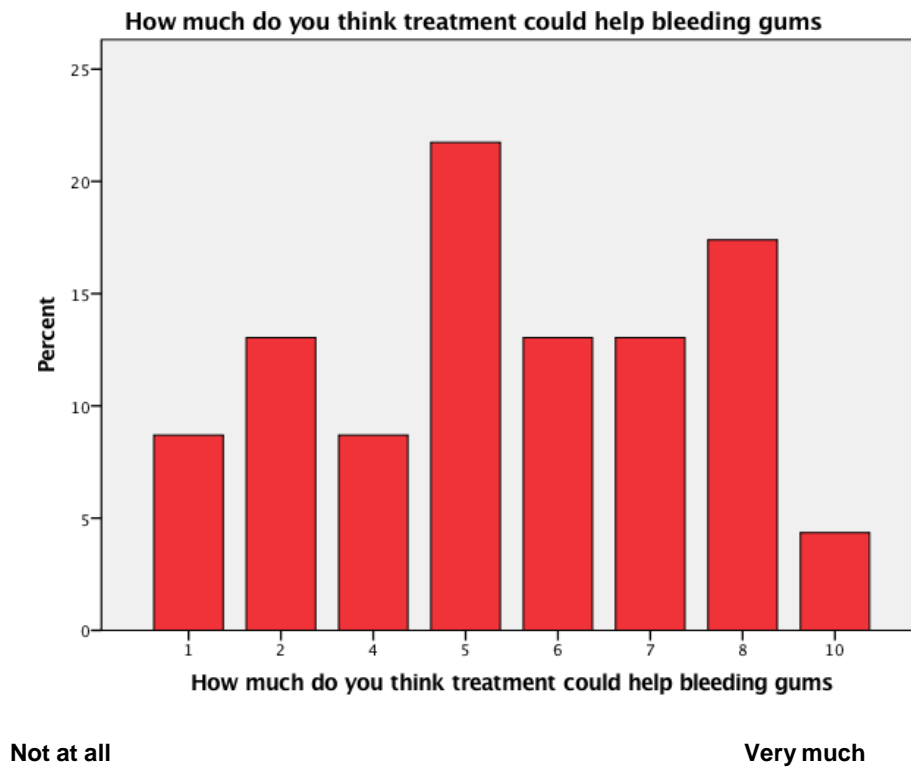


Figure 24 "How much do you think treatment could help bleeding gums?" N= 24 mean 5.1 (SD 2.6)

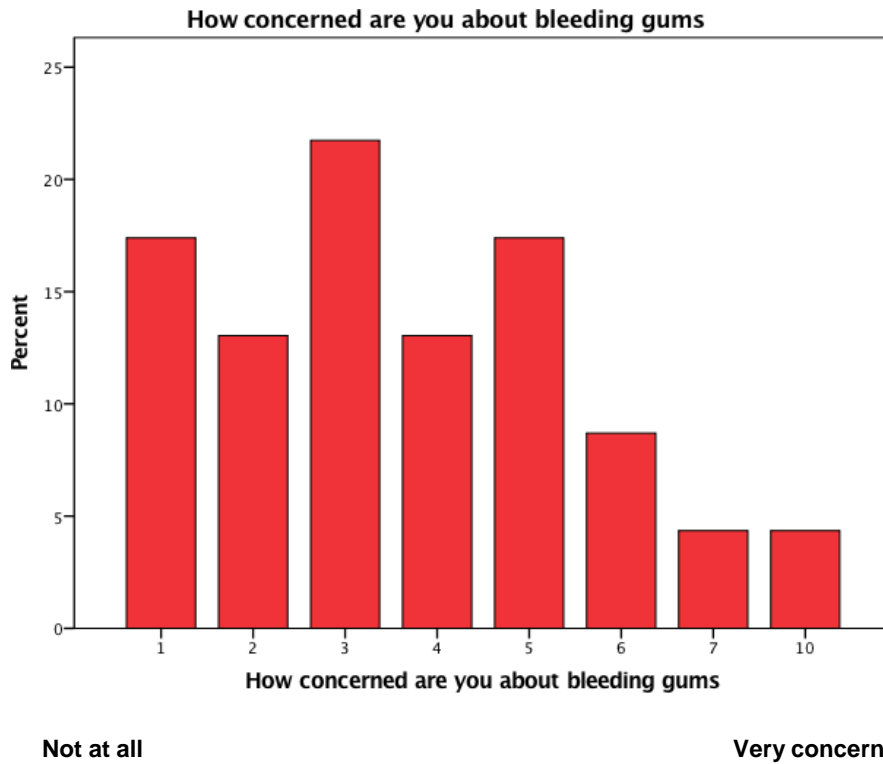


Figure 25 "How concerned are you about bleeding gums?" N = 24 mean 3.6 (SD 2.2)

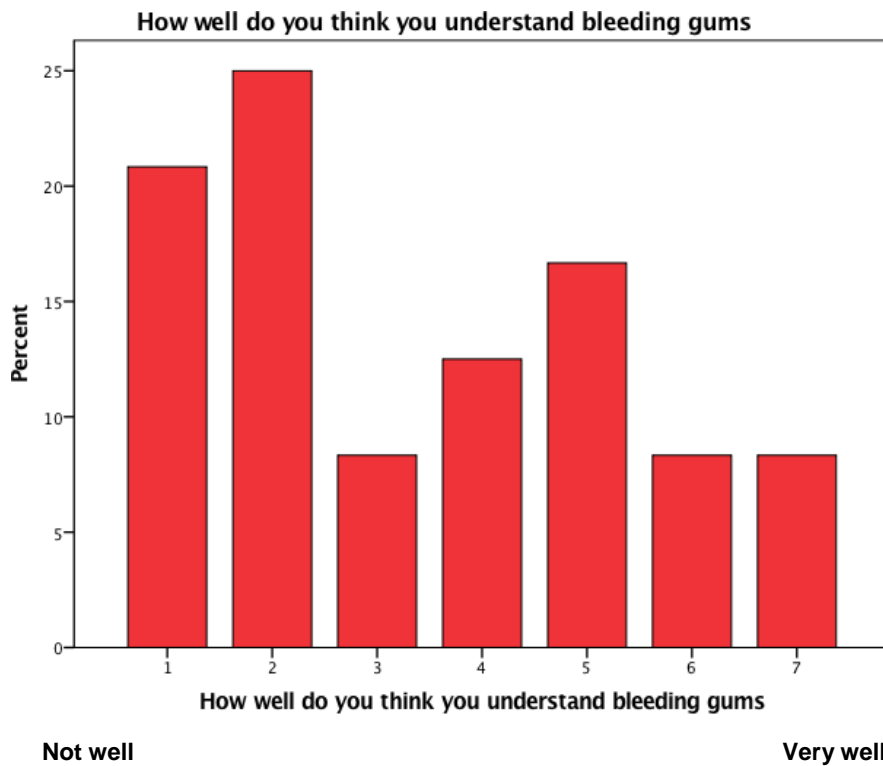


Figure 26 "How well do you think you understand bleeding gums?" N= 24 mean 3.4 (SD 2)

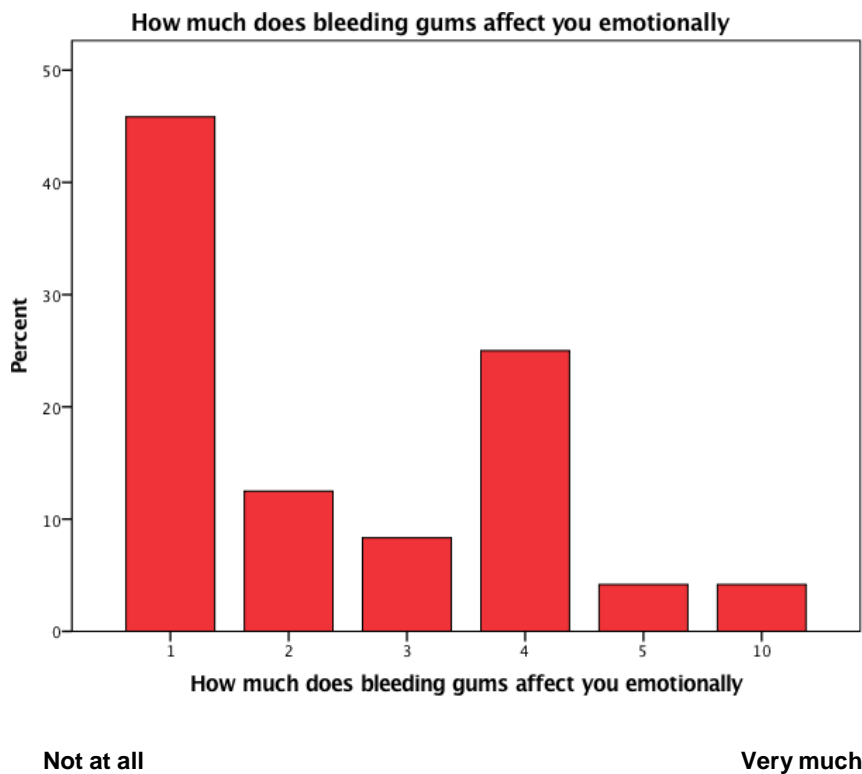


Figure 27 “How much does bleeding gums affect you emotionally?” N = 24 mean 2.6 (SD 2.1)

4.4.8 Attribution of three important factors causing gums to bleed

Nearly half of those surveyed reported that one of the most important factors that causes gingival bleeding to be brushing (20%; n=5) and brushing with a hard brush (20%; n=5), flossing (17%; n=4), and the remainder were reported that “washing teeth”, “gum disease”, “tooth decay”, “rough interspaces”, “plaque”, “menstrual cycle”, “lack of cleaning and hygiene”. These responses were elicited from participants using free text.

4.4.9 Would you seek help from your dentist about your bleeding gums?

Patients were asked to respond as to whether they would seek help from their dentists for bleeding gums. Almost one third (29%; n=7) of those surveyed responded that they would not seek help from their dentists about bleeding gums.

4.5 Clinical results

Plaque was disclosed and measured with QHI (M). Half of the individuals presented with a moderate plaque score, over than one third had a low score and the remainder were recorded with a high plaque level (Figure 28).

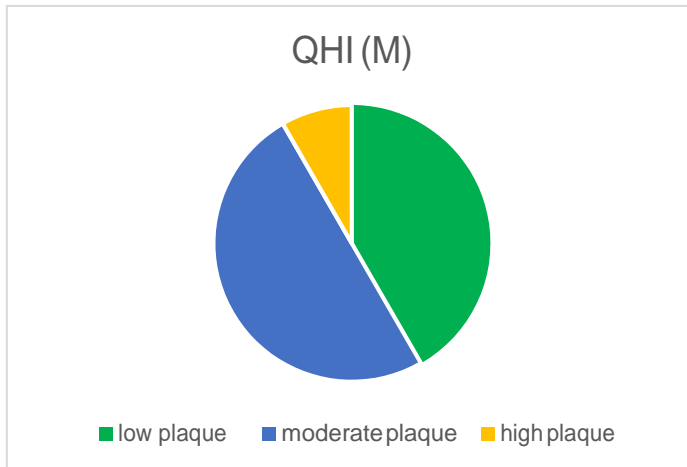


Figure 28 QHI (M) Baseline N = 24

Gingival bleeding was measured with GI (Loe & Silness, 1963) and MPBI (by Barnett *et al.*, 1980) indices. GI is a partial score using index teeth. The MBPI assesses all papillary sites for bleeding. Using the GI index, most of the patients demonstrated mild gingivitis (75%; n=18). Moderate gingivitis was recorded in 25 % (n=6) of the individuals (Figure 29). The mean GI at baseline assessment was 0.4 and SD 0.7. Mean score of MPBI at baseline assessment was 7.3 and SD was 7.2. Figure 30 illustrates the distribution of the “Worst score obtained by participant”.

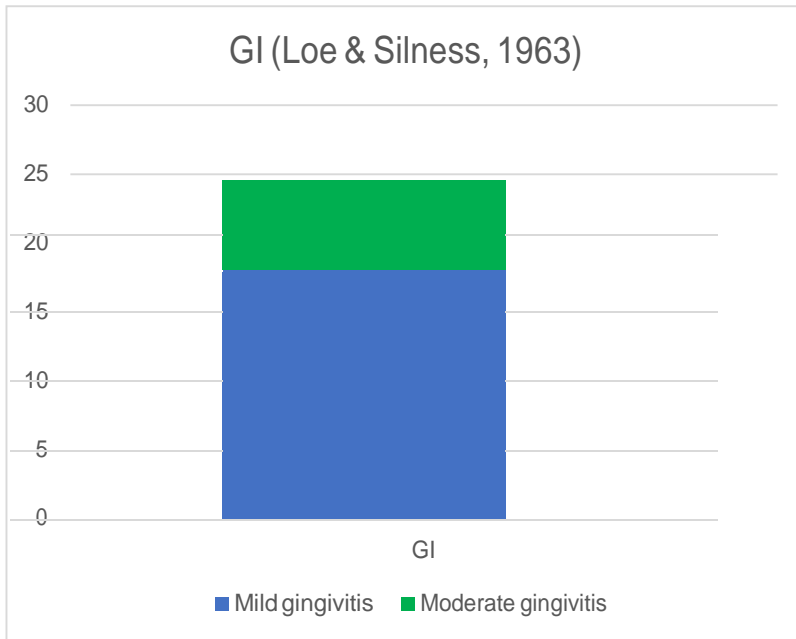


Figure 29 Gingival bleeding (Baseline) N = 24

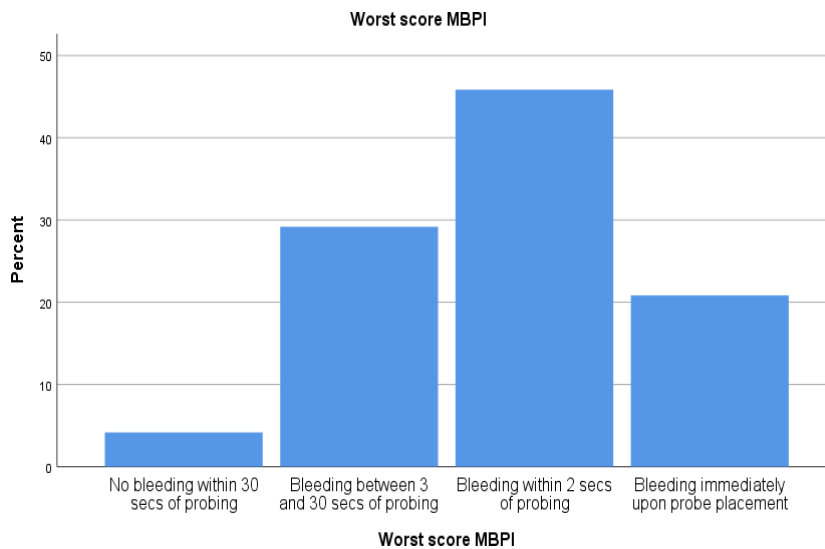


Figure 30 Worst score MBPI N = 24

4.6 Clinical measures of vWD

The clinical measures of vWD were recorded. Blood levels for vWD Ag and Rco were respectively: mean vWD Ag was 0.5dl/g SD 0.2 and for vWD Rco 0.4 dl/g

SD 0.1. This indicated that participants had low levels of vWD markers. Levels between 0.3-0.5dl/g are still associated with a bleeding phenotype (Lavin et al 2012)

4.7 Bivariate analyses

GI and plaque score had a small correlation which was not significant: Spearman's $\rho=0.374$; $N=24$; $p=0.700$. MBPI and plaque score had a moderate correlation which was not significant: Pearson correlation = 0.401 ; $N=24$; $p=0.052$.

The correlation between GI and MBPI showed good correlation and was statistically significant indicating that both measures were assessing the same phenomenon: Spearman $\rho=0.679$; $N=24$; $p=0.001$

To assess the relationship between objective and subjective measures of bleeding gums (i) Two variables were assessed using GI as a categorical variable (mild, moderate and severe gingivitis) and self-report of frequency of bleeding dichotomised into infrequent and neither infrequent nor frequent, and frequent using the bleeding question item from the IPQ score.

There was no association between perception of frequency of bleeding gums and objective measure of gingivitis GI (Chi square= 0.000 $df=1$ $p=1.00$), indicating no relationship between objective and subjective measures. There was no association between MPBI and self-perception of bleeding gums: $MW=61.500$ $p=0.616$.

To assess the relationship between (ii) measures of gingivitis (GI) (used as a continuous variable) and bleeding disorder two markers of vWD were correlated respectively. No significant association was identified for either marker:

Pearson correlation =0.004, $p=0.985$ for vWF AG and Pearson correlation=-0.040, $p=0.851$.

Similarly, no correlation was found between MBPI and two markers of vWD when they were correlated respectively. No significant association was identified for either marker: Pearson correlation =0.004, $p=0.984$ for vWF AG and Pearson correlation=-0.76, $p=0.412$.

Chapter Five: Discussion

5.1 Overview of the findings

The achieved recruitment rate to date for this study was 43% (N=24), and the results must be interpreted within this limitation. Only two participants were excluded from this study, their BPE on examination was higher than score 2. All patients with Low vWD and Type I vWD attending for their annual review were invited to participate. To the best of our knowledge the gatekeeper approached all participants with correct International Classification of Diseases (ICD) (D68002, D68003, D68007, D68008, D68009). The enrolment was slow possibly due to participants personal circumstances such as long travelling times, work arrangements, family circumstances etc.

The study is cross sectional study using quantitative methods. The data were collected using a self-report questionnaire assessing participant's health behaviours and perception of gingival health status. Participant's knowledge, beliefs and behaviours were also recorded.

The study found that people mostly rated their general health (92%) and oral health (71%) respectively as "good and very good", but a proportion (19%) only considered their oral health to be "fair". The assessment of OHRQoL gave some insight into the global self-rating of oral health. People reported they experienced a mean 3.2 impacts per person with the most frequent impacts related to four items: painful aching in the mouth (42%); difficulty in relaxing (42%); discomfort when eating (37.5%) and felt tense (37.5%). When people were asked to specifically identify the factors contributing to reduced quality of life (through free

text self-report) three main issues were reported: toothache (65%), tooth sensitivity (50%) and bleeding gums (33%). The self-report of problems and OHRQoL were aligned in cause (pain) but it is notable the 'bleeding gums' also emerged as a factor contributing to decreased quality of life in the 'free text'. A limitation of the OHIP-14 scale (Spencer *et al.*, 2007) is that it does not specifically inquire into bleeding gums. However, OHIP-14 mean and range figures are similar to a small London study of people with CBD who only report means and range (Moosajee *et al.*, 2013).

In relation to health behaviours, participants were assessed through self-report via questionnaire and this included smoking status, experience of dry mouth, dental cleaning patterns, dental attendance and dental anxiety. There were no current smokers in the sample elicited. Smoking could have potentially decreased the rates of gingival bleeding seen (Bergstrom *et al.*, 2008). The extent of perception of 'dry mouth' may also have had an impact on gingival health though only n=3 reported that it had occurred 'very often'. Participants self-reported good oral hygiene habits which were in line with current evidence-based recommendations (Public Health England, 2014). This is in contrast to findings from the UK (Fiske *et al.*, 2002 and Moosajee *et al.*, 2013). Most participants (67%) reported that they brushed their teeth twice daily and a further 21% reported more frequent brushing than this. There was widespread use of additional aids with mouthwash (71%) and flossing (46%) being the most popular. Given the self-report of oral hygiene practices, it is somewhat surprising to note the rates of plaque accumulation and gingival bleeding observed during the clinical examination described later in this section. This is more in line with the

clinical objective assessment reported by Fiske *et al.*, 2002 and Moosajee *et al.*, 2013. Dental attendance patterns also produced some conflicting data. Almost two thirds of respondents said they went regularly to the dentist (every six months) but over half (58%) reported that should they need to attend tomorrow they felt they would have a dental treatment need, which is surprising given the high rates of reported dental attendance. Only one person raised a concern about their vWD status and going to the dentist. It is interesting to note that most participants (71%) were happy with the dental care they received. Levels of dental anxiety were mostly mild and moderate with a small proportion of people reporting a dental phobia according to the MDAS scale (Humphris *et al.*, 1995). This sample of patients were attending primary care dentists for routine dental care and did not access special care dental services at St James Hospital. Their attendance patterns were more favourable than similar studies undertaken in the UK.

Participants were asked to report their experience of bleeding gums. The items used to assess experience were drawn from a series of questions exploring frequency, spontaneity, bleeding on brushing and flossing (Mohd *et al.*, 2017). The relative distributions (Figures 17, 18, 19) demonstrate that while mean scores are all midrange between “never” and “very often”, there were some individuals reporting frequency of bleeding gums. The incidence of bleeding gums on brushing and flossing reported were at the more frequent end (Figure 19). This is similar to a study by Hitchings (2012) where the majority of people reported bleeding from the mouth after flossing. However, figure 18 showed that participants in the present study almost never experienced spontaneous gums

bleeding. People were also asked specifically about the impact of bleeding gums on their life and emotions and most reported this was rare (Figure 21 and 27). It was notable that a bigger proportion of participants felt they had very little control over their bleeding gums (Figure 23). The majority were not concerned about bleeding gums and reported that they had little understanding of bleeding gums (Figure 25 and 26). Evidence for participants relating bleeding gums to dental causes is illustrated by the fact that most felt that treatment would help bleeding gums (Figure 24). Participants also attributed bleeding gums (in free text self-report) to tooth brushing techniques and types of toothbrush. Only one person attributed bleeding gums to a systemic cause (menstrual cycle). This finding differs from a report from Moosajee *et al.*, 2013 in which authors concluded that patients attributed their bleeding from gums to the bleeding disorder. Moosajee *et al.*, 2013 recruited participants with a range of CBD, while the present study only reports on vWD.

The objective clinical measures showed that two thirds of participants had moderate and high accumulations of plaque, which was well aligned to the levels of mild (75%) and moderate (25%) gingivitis recorded. There is strong biological plausibility for the presence of plaque as an aetiological agent. This was further supported by the level of bleeding reported through the MPBI score (7.3). Possibly a more relevant observation in MPBI is the 'worst score' per person as in over 20% of patients bleeding was observed immediately upon probe placement; however almost all experienced some sort of bleeding when probed. This is similar with findings from Hitchings, 2012 where she reported that the majority people bled on probing. Bivariate analyses showed a small to moderate

correlation between plaque levels and GI and MBPI respectively, but this was not significant. The under powering of the sample may have confounded the relationship. In contrast there was no correlation between objective measures of gingival bleeding and objective markers of low vWD suggesting there was no relationship between bleeding disorder and gingival bleeding. Weickert *et al.*, 2014 in a case control study also failed to find significant differences in bleeding on probing between controls and vWD.

This was the first study in Ireland to ask a sample of people living with vWD about their experience of bleeding gums, and there is no control to compare with the general population. Nevertheless, rates of concerns about bleeding are less than reported by Hitchings (2012). Although her study looked at a range of CBD. It is a long held view of dentists that people with CBD do not brush their teeth because of attributing dental bleeding to their CBD (Fiske *et al.*, 2002 and Hitchings (2012) for example). This was not borne out in the present study as most participants did not display concern about bleeding gums and only one person reported having low vWD as a barrier to going to the dentist. Another possible explanation might be that the level of bleeding gums was 'normal' to this population who are habituated to other types of bleeding such as heavy periods or nose bleeds.

From literature review we clearly see there is a tendency for all bleeding disorders to be rolled into the one big group of CBD. Even though vWD is the most common bleeding disorder there have been only a few studies that looked specifically at vWD. This group is also typically characterised by mucocutaneous bleeding in comparison to Haemophiliac patients where they bleed into their joints etc. the

more “obvious” parts of the body. It seems that this larger vWD population is hugely overlooked. The preliminary results from this study show no relation between participants’ perception and attribution of cause and experience of their bleeding gums. However, it is important to recognise and understand beliefs and values in order to change oral behaviours.

The strength of this study is this is a population group that is not well studied or understood. Our study provides insights into beliefs and behaviours which will help to form oral health promotion interventions.

5.1.1 Limitations of the study

The response rate was low at 43% and so the results should be interpreted with caution. Nevertheless, the participants were a consecutive sample of people attending the OPD and may well reflect people living with vWD in Ireland. Participants in the study displayed low levels of vWD (0.5 dl/g) but while not severe they were sufficient to present a significant bleeding phenotype in other areas ie nose bleeds, heavy periods etc.

Much of the data collected during the study relied on self-report and there may be an important bias there due to social desirable responding. This may have been particularly relevant when asking about oral hygiene practices, as most reported optimal oral hygiene yet objective measures of plaque measurement showed high levels of accumulation suggesting that while frequency was optimal the technique or use of aids was not. A similar issue may well have occurred in relation to dental attendance pattern where participants reported regular and recent attendance yet appeared to experience dental pain and a range of dental

problems. These were validated during the OHIP-14 assessment as well. Levels of dental phobia were similar to population levels reported in a small study in Cork (Brady *et al.*, 2012), and so were unlikely to explain anomalies in reported dental attendance. No individual cited their bleeding disorder as a barrier to care. The most likely explanation is social desirable responding.

The study also relied on self-report for 'bleeding gums' but this was assessed a number of times through the OHRQoL free text and through specific questions on perception of bleeding. Both assessments aligned with each other and indicate that the assessment of perception was an accurate reflection of participant's views. Participants reported that they had little understanding of why gums bleed and were unlikely to have developed coherency in answers to achieve social desirable understanding.

Finally, an important limitation is measuring bleeding in the context of a bleeding disorder. No clinical examination identified mucocutaneous bleeding though the sample did not contain participants at the severe end of vWD. The GI has been used widely in pre- and post-test studies assessing change in gingivitis. It is however a partial score and does not give timing of bleeding. MBPI was chosen because it was a total score and had the advantage that the timing of bleeding was reported. Unfortunately, because there was no 'population' control it is not possible to estimate whether bleeding lasted longer in people with low vWD.

Chapter Six: Conclusion

- Most participants rated their oral health as 'good and very good' yet all reported reduced oral health related quality of life in four areas: painful aching in the mouth (42%); difficulty in relaxing (42%) discomfort when eating (37.5%) and feeling tense (37.5%). Self-report of oral problems were: toothache (65%), tooth sensitivity (50%) and bleeding gums (33%).
- While participants reported optimal oral hygiene practices, objective clinical measures showed high plaque accumulation and mild (75%) and moderate gingivitis (25%).
- Most participants acknowledged that they had little understanding of why their gums bled but felt that treatment (dental) would be beneficial.
- There was an insignificant small to moderate correlation between plaque levels and GI and MBPI respectively. There was no correlation between objective measures of gingival bleeding and objective markers of low vWD suggesting there was no relationship between bleeding disorder and gingival bleeding.
- There is no association between gingival bleeding and vWD factor.

Chapter Seven: Recommendations

- Oral hygiene interventions are warranted in this population subgroup.
- There is a need for evidence based oral hygiene interventions personalised to this group population given the context of their bleeding disorders.
- Future studies should consider the developing protocols for professional hygiene interventions in the population group.
- In order to remove bias, future studies should consider comparing gingival bleeding levels in vWD and matched to a healthy control.

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Patient Information Leaflet Version 1 September 25, 2017

Title of the study: Presence and impact of bleeding from the mouth in people living with Low Von Willebrand Factor in Ireland

Introduction

You are being invited to take part in a research study. It is a local study that will involve patients at the National Coagulation Centre. Before you decide whether you wish to be involved, it is important for you to understand why the research is being done and what it will entail. Please, take time to read the following information carefully and discuss it with your family and GP if you wish so. Ask us if there is anything that is not clear or if you would like to get more information. Take time, whether or not you wish to take part. Thank you for taking your time to read this.

What is the purpose of the study?

Von Willebrand disease (VWD) is associated with a bleeding tendency, and is caused by reduced levels of the blood clotting protein von Willebrand factor (VWF). Some people with low VWF report they experience bleeding from the mouth, but the reason for this bleeding is not well understood. In this study we want to see if bleeding from the mouth might be related to reduced VWF or to gum disease.

Why have I been chosen?

You have a personal diagnosis of having reduced von Willebrand factor levels. By involving you in the study we hope to identify people with low VWF who have experienced bleeding gums and observe whether this bleeding is related to reduced VWF or to gum disease.

Procedures

If you kindly agree to participate in the study, we shall ask you to sign a consent form and give you an appointment to return for a dental assessment, which may involve a dental cleaning. This appointment will involve a short questionnaire (by ipad or paper) that will ask you about your teeth and gums, and how you look after them (ten minutes).

The short interview will be followed by a dental assessment of your gum health (25 minutes, less if you have few remaining teeth). We shall assign you randomly to one of two groups. One group will have their teeth professionally cleaned (30 minutes) and then you will be shown how to clean your teeth and gums (10 minutes). We shall follow a cleaning protocol agreed by your haematologist. The second group will also be shown how to clean their teeth and gums (10 minutes), but will not have their teeth professionally cleaned at this visit. We shall ask you to return for a second visit when we will ask you to complete a second questionnaire and have your gum health assessed again. Those who did not receive a complimentary tooth cleaning at the first visit will receive it at the second visit.

In total, the study procedures will add an additional 10 minutes to your complimentary hygienist review and visit.

Version 1.0 Participant Information Sheet

Title of the study: Presence and impact of bleeding from the mouth in people living with Low Von Willebrand Factor in Ireland 25 Sept September 2017

With your permission, we shall extract your LWD factor blood levels, your ISTH BAT and condensed MCMDM-1 VWD scores from your medical records. This will help us compare our dental findings with your levels of VWD factor.

What are the possible benefits of taking part?

We hope to find the reason for reported bleeding in the mouth and to offer a solution for this. You would not directly benefit from this study, but it could help our understanding of the reasons for bleeding gums in people with reduced VWF. As part of the study, you will receive a complimentary tooth cleaning and polishing.

Please note: patients will not receive a comprehensive dental examination during the proposed study. However, if an oral health condition is apparent to the Dentist, the participant will be advised to contact their general dental practitioner for comprehensive oral examination or management of periodontal disease. Apart from two sessions of tooth cleaning, no dental treatment or ongoing dental care will be offered or provided, as is the normal process for patients attending the NCC with Low VWF.

What are the possible disadvantages and risks of taking part?

Entering this study will not affect your normal treatment in any way.

Exclusion from participation:

If you have any of the following conditions you will not be suitable to take part. Many thanks for taking the time to read this leaflet.

Current smokers
Diabetics
Individuals taking antibiotics by mouth
Pregnant or suspect you may be pregnant

Alternative treatment:

If you do not wish to take part in this study, you will continue under the care of your treating physician and / or surgeon, and your routine clinical care will remain unchanged.

Confidentiality:

All information that is collected about you during the course of the research will be kept strictly confidential. You will be allocated an individual study number.

Compensation:

Nothing in this document restricts or curtails your rights. **The research team will not alter your treatment in any way during their conduct of the study; we do not anticipate you experiencing any harm from taking part.** However, if taking part in this research projects harms you, there are no special compensation arrangements.

Voluntary Participation :

Your participation in the study is entirely voluntary. You are free to decline to enter or to withdraw from the study at any time without having to give a reason. If you choose not to enter the study, or withdraw once entered, this will in no way affect your future medical care. If you decide to take part you will be given this information sheet to keep and asked to sign a consent form.

Version 1.0 Participant Information Sheet

Title of the study: Presence and impact of bleeding from the mouth in people living with Low Von Willebrand Factor in Ireland 25 Sept September 2017

Stopping the study:

When the study comes to the end, the data will be analysed by the Research team and by an experienced Medical Statistician. Anonymised, aggregated data will be published to inform the wider community of doctors and dentists treating patients with bleeding disorders. All data will be coded and anonymised and you will not be identifiable.

Permission:

The study has been reviewed and approved by the Local Hospital Research Ethics Committee (LREC)- The SJH/AMNCH Research Ethics Committee.

Further Information:

If you have any queries, you can contact.....

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Email: ncc@stjames.ie

Version 1.0 Participant Information Sheet

Title of the study: Presence and impact of bleeding from the mouth in people living with Low Von Willebrand Factor in Ireland 25 Sept September 2017

Appendix 2



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



Chief Investigators: Dr. Alison Dougall,
Local Study Co-ordinator: DR Alison Dougall
Phone No: 01 4162141
Fax No: 01 4103517

**Consent / Assent Form: Presence and impact of bleeding from the mouth
in the people living with Low Von Willebrand Factor in Ireland**

This study and this consent form have been explained to me. My researcher has answered all my questions to my satisfaction. I believe I understand what will happen if I agree to be part of this study. I have read, or had read to me, this consent form. I have had the opportunity to ask questions and all my questions have been answered to my satisfaction. I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights. I have received a copy of this agreement.

PARTICIPANT'S NAME: _____

PARTICIPANT'S SIGNATURE: _____

Date: _____

Date on which the participant was first furnished with this form: _____

Where the participant is incapable of comprehending the nature, significance and scope of the consent required, the form must be signed by a person competent to give assent to his or her participation in the research study (other than a person who applied to undertake or conduct the study).

NAME OF PARTICIPANT: _____

SIGNATURE: _____

Where the participant is capable of comprehending the nature, significance and scope of the consent required, but is physically unable to sign written consent, signatures of two witnesses present when consent was given by the participant to a registered medical practitioner treating him or her for the illness.

NAME OF 1st WITNESS: _____ SIGNATURE: _____

NAME OF 2nd WITNESS: _____ SIGNATURE: _____

Statement of Investigator's responsibility: I have explained the nature, purpose, procedures, benefits, risks of, or alternatives to, this research study. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

Researchers's signature: _____ Print name _____

Date: _____

(Original copy to patient notes; One copy to patient; One copy to be kept in study folder)

Presence of bleeding from the mouth study consent form

Version 1.0

Dated 27th Sept 2017

Page 1 of 1

Appendix 3



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



Baseline Questionnaire Version 1.1 23 February 2018

[The interface used will be survey monkey an on-line web based tool, using survey monkey formats.]

Title of Study: Presence and impact of bleeding from the mouth in people living with low levels of Von Willebrand's factor: gingivitis or mucocutaneous bleeding?

You are invited to participate in a short questionnaire to answer some questions about your dental health, going to the dentist and your experience of bleeding gums. Your responses are important, and we are interested in your views. There are no right or wrong answers to these questions. Ask us if there is anything that is not clear or if you would like to get more information.

Please complete the questionnaire on the following pages:-

The questionnaire should take no longer than 15 minutes to complete. Hand the paper questionnaire to the research coordinator when you have completed the questionnaire. All responses will be treated confidentially.

Thank you for taking the time to take part.

Further Information:

If you have any queries, you can contact

Name: Dr. Alison Dougall
Address: National Coagulation Centre, St. James's Hospital
Telephone: 01 4162141
Fax: 01 4103570
Email: ncc@stjames.ie

Participant code

<p>1 Health questions</p> <p>How is your health in general; would you say it was...</p> <p>very good <input type="checkbox"/>_1, good <input type="checkbox"/>_1, fair <input type="checkbox"/>_1, bad <input type="checkbox"/>_1, or very bad? <input type="checkbox"/>_1</p> <p>(And) would you say your dental health (mouth, teeth and/or dentures) is...</p> <p>Running prompt</p> <p>very good <input type="checkbox"/>_1, good <input type="checkbox"/>_1, fair <input type="checkbox"/>_1, bad <input type="checkbox"/>_1, or very bad? <input type="checkbox"/>_1</p>

2 Oral health related quality of life....

In the last 12 months have you experienced the following because of problems with your teeth mouth and gums	Never	Hardly ever	Occasionally	Often	Very often
1 Trouble pronouncing words	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
2 Felt sense of taste worsened	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
3 Had a painful aching in the mouth	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
4 Found it uncomfortable to eat any food	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
5 Have been self conscious	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
6 Felt tense	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
7 Had an unsatisfactory diet	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
8 Had to interrupt meals	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
9 Found it difficult to relax	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
10 Have been a bit embarrassed	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
11 Have been irritable with other people	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
12 Had difficulty doing usual jobs	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
13 Life in general was less satisfying	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅
14 Have been totally unable to function	<input type="checkbox"/> ₁	<input type="checkbox"/> ₂	<input type="checkbox"/> ₃	<input type="checkbox"/> ₄	<input type="checkbox"/> ₅

3. Which one of the following oral conditions has caused this difficulty ...ACTIVITY / BEHAVIOR...?). Please circle all that apply.

toothache	1	receding gums	11
sensitive tooth	2	tartar	12
tooth decay (hole in tooth)	3	oral ulcer or spot	13
fractured tooth	4	bad breath	14
tooth loss	5	deformity of mouth or face (e.g. cleft lip, cleft palate)	15
loose tooth	6	clicking or grating noise in jaw	16
colour of teeth	7	improper filling or crown (e.g. broken, col-our)	17
position of teeth (e.g. crooked or projecting, gap)	8	loose or ill-fitting denture	18
shape or size of teeth	9	orthodontic appliance	19
bleeding gums	10	or any other reason? (please specify)	20

4 Smoking

Smoking (Yes would include at least once ever)

Have you ever smoked a cigarette, a cigar, or a pipe?

Yes No please, give details _____

If respondent answered 'Yes' then ask

And do you smoke cigarettes, a cigar or pipe at all nowadays?

Yes No

5 Diet

How often, on average do you have fizzy drinks, fruit juice, or soft drinks like squash, excluding diet or sugar-free drinks?

6 or more times a week 3-5 times a week 1-2 times a week Less than once a week Rarely or never

Do you usually have sugar in hot drinks like tea and coffee? [If the respondent uses artificial sweetener, code No]

Yes No Does not drink hot drinks

6 Dry mouth
How often does your mouth feel dry?
 never, hardly ever , occasionally fairly often very often

If you answered occasionally, fairly often and very often, are there things you do to moisten your mouth and alleviate the symptoms?
 Describe _____

7 Teeth and Denture Cleaning
How often do you clean your teeth nowadays? (Question refers to brushing only)
 More than twice a day , Twice a day, Once a day , Less than once a day Never

....(And) do you have a denture (Y/N)
 • Yes • No

If yes how often do you clean your dentures nowadays?
 More than twice a day, Twice a day, Once a day, Less than once a day Never

Do you have a toothbrush? Yes No

Do you have toothpaste? Yes No

Do you use anything other than an ordinary (manual) toothbrush and toothpaste for dental hygiene purposes? E.g. electronic toothbrush, chewing gum, code yes).
 Yes No

If Yes does it include you can tick more than one answer
 Dental floss Interdents/toothpicks/woodsticks Mouthwash Interspace brush
 Electric toothbrush Denture cleaning solution Sugar-free chewing gum
 Something elseif this please record what it is here _____

Which brand of toothpaste do you currently use (most often)? _____

8 Teeth and dentures
Do you have (require) a denture, even if you don't wear it?
 Yes No

9 Dental Attendance

If you went to the dentist tomorrow, do you think you would need any treatment?

Yes No

If yes, what do you think you might need to have done? Please describe

Description.....for example fillings, denture etc

In general do you go to the dentist for...

a regular check up, an occasional check up, or only when you're having trouble with your teeth/dentures?

Never been to the dentist -

How often do you go to the dentist? Is it...

at least once every six months, at least once every year, at least once every two years, or less frequently than every two years? or only when having trouble with your teeth and/or dentures? -

About how long ago was your last visit to the dentist? (This is the last visit at which you visited a dentist –it does not include a visit to the dental hygienist)

Within the last 6 months Within the last 7-12 months More than 1, but less than 2 years ago More than 2, but less than 3 years ago More than 3, but less than 5 years ago More than 5, but less than 10 years ago

More than 10 years ago

, which of these, if any, are the reasons why you have not been to the dentist in the last two years? [You may tick more than one option]

No need to go to the dentist/nothing is wrong with my teeth I haven't got the time to go I can't afford the charges I am afraid of going to the dentists Keep forgetting/Haven't got a chance None of these reasons

Other (please state)

...and which of these, if any, are also reasons why you have not been to the dentist in the last two years? [CODE ALL THAT APPLY]

It's difficult to get to/ from the dentist I have had a bad experience with a dentist I am too embarrassed to go to the dentist I don't see the point in going to the dentist I have been refused treatment/registration by dental practice Some other reason (please specify)

The last time you visited the dentist, what was the purpose of your visit? Was it...

for a routine check-up, for emergency or urgent treatment, or for other treatment (non-emergency, non-urgent)? Some other reason (please specify)

- **What was the other reason?** _____

There are things about the dental care I receive that could be better
 strongly agree , _1 agree, _1 not sure, _1 disagree _1 strongly disagree _1

10 Your feelings about dentistry (Humphris et al 1995)

Please tell us how anxious you get, if at all, with your dental visit. Each item is about different aspects of visiting a dentist. The scale ranges from 'not anxious' to 'extremely anxious'. For each item we would like you to tick the box that represents the how anxious you get.

	Not anxious	Slightly anxious	Fairly anxious	Very anxious	Extremely anxious
1 If you went to your Dentist for treatment tomorrow how would you feel?	<input type="checkbox"/> _1	<input type="checkbox"/> _2	<input type="checkbox"/> _3	<input type="checkbox"/> _4	<input type="checkbox"/> _5
2 If you were sitting in the waiting room (waiting for treatment), how would you feel?	<input type="checkbox"/> _1	<input type="checkbox"/> _2	<input type="checkbox"/> _3	<input type="checkbox"/> _4	<input type="checkbox"/> _5
3. If you were about to have a tooth drilled , how would you feel?	<input type="checkbox"/> _1	<input type="checkbox"/> _2	<input type="checkbox"/> _3	<input type="checkbox"/> _4	<input type="checkbox"/> _5
4 If you were about to have your teeth scaled and polished , how would you feel?	<input type="checkbox"/> _1	<input type="checkbox"/> _2	<input type="checkbox"/> _3	<input type="checkbox"/> _4	<input type="checkbox"/> _5
5. If you were about to have a local anaesthetic injection in your gum, above an upper back tooth, how would you feel?	<input type="checkbox"/> _1	<input type="checkbox"/> _2	<input type="checkbox"/> _3	<input type="checkbox"/> _4	<input type="checkbox"/> _5

**11 These questions are asking about your experience of bleeding gums
(please tick)**

1) *Have you had any experience of bleeding gums?* { mark the response where 1 is never and 10 is very often, 5 is in the middle). If you answered 'never' skip to question 3)

1	2	3	4	5	6	7	8	9	10
Never									Very often

2) *If yes, does the bleeding occur spontaneously?* { mark the response where 1 is never and 10 is very often, 5 is in the middle

1	2	3	4	5	6	7	8	9	10
Never									Very often

3) *Do your gums bleed when you brush your teeth and /or floss your teeth?* { mark the response where 1 is never and 10 is very often, 5 is in the middle).

1	2	3	4	5	6	7	8	9	10
Never									Very often

4) *Do you think it takes a long time for your gums to stop bleeding after tooth-brushing or flossing?* {ask participant to mark the response where 1 is never and 10 is very often, 5 is in the middle).

1	2	3	4	5	6	7	8	9	10
Never									Very often

If yes, how long does it take for the bleeding to stop? Please tick your preferred option.

- Less than 5 minutes
- 5 to 10 minutes
- 10 to 30 minutes
- More than 30 minutes
- A few hours

12 Perception Questionnaire (1-7)

Please grade your responses to the following statements { mark the response where 1 is not at all and 10 is extremely so, 5 is in the middle}

1 *How much do bleeding gums affect your life?*

1	2	3	4	5	6	7	8	9	10
Not At all									Extremely so

2 *For how long do you think you will experience bleeding gums?*

1	2	3	4	5	6	7	8	9	10
Not Long									A very long time

3 *How much control do you feel you have over bleeding gums ?*

1	2	3	4	5	6	7	8	9	10
Not At all									Extremely so

4 *How much do you think treatment can help bleeding gums ?*

1	2	3	4	5	6	7	8	9	10
Not At all									Extremely so

5 *How concerned are you about bleeding gums?*

1	2	3	4	5	6	7	8	9	10
Not At all									Extremely so

6 *How well do you think you understand bleeding gums?*

1	2	3	4	5	6	7	8	9	10
Not At all									Extremely so

7 *How much would you say bleeding affects you emotionally ? (e.g. does it make you angry, scared, upset or depressed?)*

1	2	3	4	5	6	7	8	9	10
Not Affected at all emotionally									Extremely affected emotionally

--	--	--	--	--	--	--	--	--	--	--

13 Please list in rank-order the three most important factors that you believe causes your gums to bleed. The most important causes for me:-

- a. _____
- b. _____
- c. _____

14 Would you seek help from your dentist about your bleeding gums?

1	2	3	4	5	6	7	8	9	10
Very unlikely									Extremely Likely

THANK YOU THIS IS THE END OF THE QUESTIONNAIRE. PLEASE RETURN TO THE RESEARCH CO-ORDINATOR

For administration purposes

Next record data re participant (most recent recording)

BPE:

GI (Loe & Silness):

MPBI:

QHI(M):

VWD Factor Blood level (IU/dl)

Bleeding score ISTH BAT.....

Condensed MCMDM-1 VWD score.....

Appendix 4

The plaque score is explained to the patient, and they are advised what causes gums to bleed and how to manage oral hygiene. The following standard text is used for all patients.

Your gums can bleed for a number of reasons. The commonest reason is a plaque around the teeth. Plaque is full of bacteria, which sticks to your teeth and gums. It builds up where the gum meets the tooth and if not removed causes the gums to be inflamed and then they start to bleed. The only way to prevent or stop this bleeding is with physical disruption (Dental Health Foundation, 2014). Evidence suggests that if you stick to a good oral hygiene routine the bleeding in your gums will stop in 2-3 weeks (Loe *et al.*, 1965). This is no different for people with low Von Willebrands. So today, we are going to use disclosing agent (vegetable dye), which will show us if you have any plaque on your teeth.

The participant is introduced to the researcher hygienist and receive a 10-minute instruction on how to clean their teeth and gums (OHI). A Home pack for oral care is provided. This includes a medium toothbrush, interdental brushes, a toothpaste, disclosing tablets, a pack of interdental floss, an oral hygiene diary and an oral hygiene leaflet. The participant is asked to undertake oral hygiene twice daily during the six-week period. Participants are also asked to complete the oral hygiene diary and bring it to the next appointment.

Patients allocated to **control group** are thanked for participation and asked to return in 8-12 weeks' time.

Patient allocated to **intervention group** receive complimentary tooth debridement (20 minutes) and standard post-operative instructions. The patient is thanked for participation and asked to return in 8-12 weeks' time for review.

At the 8-12-week visit, participants from both the control/ intervention groups are asked to complete a short (5 min) follow up questionnaire and have gum health reassessed (MPBI, GI, QHIM) 25 min by a researcher blind to group allocation.

Patients allocated to **intervention group** is thanked for participation.

Patients allocated to **control group** receive a complimentary full mouth cleaning (20 minutes); and the patient is thanked for participation.

Advised patient if any problems to contact Haemophilia Clinic. Telephone number is supplied. The patient is asked to ring Haemophilia Clinic if any adverse reactions occur up to 3 days after tooth debridement.

Appendix 5

References:

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10. Slot, D., Dorfer, C. and Van der Weijden, G. (2008) The efficacy of interdental brushes on plaque and parameters of periodontal inflammation: a systematic review. *International Journal of Dental Hygiene*, 6, 253-264.

If bleeding problems occur, please phone:
National Coagulation Centre
 (01) 416 2141 / (01) 416 2142

Daily Brushing Version 3.1 23 February 2018



Dear Participant,

Thank you for taking part in a research study. We hope that you find the information below helpful and you will find the time to incorporate into your daily routine.

Your gums can bleed for a number of reasons. The commonest reason is plaque around teeth. Plaque is an almost colourless bacterial film, which sticks to your teeth. The accumulation of plaque around the gum margins causes the inflammation. The only way to stop/control this is with physical disruption¹. Evidence suggests that if you adhere to a good oral hygiene routine the bleeding in your gums will stop in 2-3 weeks². This is no different for people with low Von Willebrand's.

Oral hygiene should be performed at night time and at one other time (of your choosing), twice a day³.

A special dye in the form of a disclosing tablet can be used to stain the plaque, thus making easier to see¹.

First, you need a soft to medium small headed (19 mm) toothbrush. Then you place a pea sized amount of fluoridated toothpaste on the toothbrush^{3,4}.

Toothpaste with at least 1450 part per million fluoride content is recommended⁵.

For the purpose of this study we will give you a recommended toothbrush.



Please, position the toothbrush firmly at 45° against the gum margin. Then commence brushing with circular motions half on the tooth half on the gum.

We would recommend you start your brushing on the right side beginning with the cheek surfaces of the top back teeth, continuing round to the front teeth and on to the cheeks side of the upper left back teeth. Then you move to the inside surfaces and work your way back to the right side.



It helps to reposition the toothbrush vertically when brushing the inside of your front teeth, as the dental arch is naturally curved here.



Then you move to the lower teeth and repeat the brushing starting with the right side back teeth cheek surfaces, on to your front lower teeth and then the left side. Then you move to the inside surfaces and work your way back to the right side.

It is important not to scrub while brushing as this can damage your gums and push them away from tooth causing gum recession⁶.



The biting surfaces of your teeth can be scrubbed, as there is no gum here and therefore gum is not affected.



The top surface of the tongue has an irregular surface, which allows bacteria to grow and multiply. The tongue should be cleaned at the end of your brushing spell⁷.



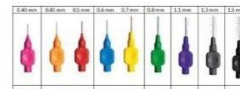
A toothbrush effectiveness reduces after 3 months of use or when it becomes splayed⁸. So, it should be replaced. A medium brush is recommended.



Brushing should take at least 2 minutes¹. We suggest you set a timer on your phone or other device. You can also download and install an app on your phone. For instance, The Brush DJ oral health app is available to download at <http://www.brushdj.com/>



Dental floss or interdental brushes remove plaque and retained food between teeth. The toothbrush cannot reach those spaces. Dental floss is used for crowded/tight spaces, but interdental brushes are more effective for larger spaces/gaps^{9,10}.



Personalised PS

Personalised BI

Appendix 6




Tooth Brushing and Interdental Cleaning Chart


This chart is developed for a study that involves patients with bleeding disorders at the National Coagulation Centre. The most important plaque control method is toothbrushing and interdental cleaning. Evidence suggests that if you adhere to a good oral hygiene routine the bleeding in your gums will stop in 2-3 weeks (Loe et al., 1965).

We would like you to implement this chart into your oral hygiene routine. Please, tick the boxes when you carry out brushing and interdental cleaning. We would appreciate if you bring this chart for your next appointment.

	Week 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	Morning /Afternoon	Night	Morning /Afternoon	Night	Morning /Afternoon	Night	Morning /Afternoon	Night	Morning /Afternoon	Night	Morning /Afternoon	Night
Monday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tuesday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Wednesday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Thursday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Friday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Saturday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sunday	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



1 Please, position the toothbrush firmly at 45° against the gum margin. Then commence brushing with circular motions half on the tooth half on the gum.



2 Dental floss or interdental brushes remove plaque and retained food between teeth. The toothbrush cannot reach those spaces. Use a gentle motion to guide the floss between teeth and then gently move the floss inside the gum and up. If using interdental brushes, please choose appropriate size to insert between your teeth and push it gently in and out a few times.

Personalised PS

Personalised BI

Version 1.4 23 February 2018

Appendix 7



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



Case Report Form 2.2 15 February 2018

This is a dental charting for a participant with code _____. This chart is developed for a local study that involves patients with bleeding disorders at the National Coagulation Centre. The name of the study is "Presence and impact of bleeding from the mouth in people living with von Willebrand factor: gingivitis or mucocutaneous bleeding?". The dental charting includes recording of **Quigley Hein Index (modified)**, **BPE** and **Gingival Index (Loe & Silness, 1963) GI**.

1) BPE

Included in the study

Excluded from the study

2)MPBI 3)GI 4)PI

	Buccal																						
	MPBI																						
	PI																						
	GI																						
	Lingual																						
	MPBI																						
	PI																						
	GI																						

	Buccal																						
	MPBI																						
	PI																						
	GI																						
	Lingual																						
	MPBI																						
	PI																						
	GI																						

DENTAL ASSESSMENT LOVIC

2. Modified Papillary Bleeding Index
 (Total score) =

3. Gingival Index (Loe & Silness, 1963)
 Total Score =
 Number of surfaces examined =
Final Score = Total Score/no. of surfaces) =

0.1-1 Mild gingivitis	
1.1-2 Moderate gingivitis	
2.1-3 Severe gingivitis	

4. Quigley Hein Index (modified)=
 Total score =
 The number of surfaces examined =
Final Score = Total Score/no. of surfaces) =

0-1 is low	
≥ 2 is high	

The charting is copied and stored with patient's medical chart by Ms Parkinson.

Date